HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

Overview clinica sul ruolo della IMRT: Head and Neck

Paolo Antognoni
U.O. RADIOTERAPIA
Ospedale di Circolo e Fondazione Macchi
VARESE

Giuseppina De Marco
U.O. RADIOTERAPIA ONCOLOGICA
Dipartimento Integrato di Oncologia ed Ematologia
Azienda Ospedaliero-Universitaria Policlinico
MODENA

Aifm
Associazione Italiana di Fisica Medica

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

VANTAGGI DELLA IMRT IN HEAD & NECK

- Maggior risparmio di vari OARs (parotidi, midollo spinale, bulbo, chiasma, nervi ottici…): PTV concavi
- Possibilità di dose escalation
- Possibilità di somministrazione contemporanea di livelli di dose differenziati per irradiare simultaneamente le sedi di malattia macroscopica e quelle con presunta malattia subclinica (SIB-IMRT)

INDIAN J CANCER **Year** : 2010 | **Volume** : 47 | **Issue** : 3 | **Page** : 267-273

The role of intensity-modulated radiotherapy in head and neck cancer
SA Bhide, R Kazi, K Newbold, KJ Harrington, CM Nutting
Head and Neck Unit, The Institute of Cancer Research and The Royal Marsden Hospital, London and Surrey, United Kingdom

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

IL "BACKGROUND": LA RICERCA DELLA NUOVA FRONTIERA…

"The use of multiple static beams, each broken into two or more segments whose intensity varies according to the plan's objectives, is a simple example of intensity modulated radiation therapy"

1998 — **Basi tecnologiche**

Int. J. Radiation Oncology Biol. Phys., Vol. 41, No. 3, pp. 559–568, 1998
Copyright © 1998 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/98 $19.00 + .00
PII S0360-3016(98)00082-0

● *Clinical Investigation*

COMPREHENSIVE IRRADIATION OF HEAD AND NECK CANCER USING CONFORMAL MULTISEGMENTAL FIELDS: ASSESSMENT OF TARGET COVERAGE AND NONINVOLVED TISSUE SPARING

AVRAHAM EISBRUCH, M.D.,* LON H. MARSH, R.T.T.,* MARY K. MARTEL, PH.D.,* JONATHAN A. SHIP, D.M.D.,† RANDALL TEN HAKEN, PH.D.,* ANTHONY T. PU, M.D.,* BENEDICK A. FRAASS, PH.D.,* AND ALLEN S. LICHTER, M.D.*

1999 — **Applicazione del SIB/SMART**

Int. J. Radiation Oncology Biol. Phys., Vol. 45, No. 1, pp. 21–32, 1999
Copyright © 1999 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/99/$–see front matter
PII S0360-3016(99)00101-7

CLINICAL INVESTIGATION — Head and Neck

SMART (SIMULTANEOUS MODULATED ACCELERATED RADIATION THERAPY) BOOST: A NEW ACCELERATED FRACTIONATION SCHEDULE FOR THE TREATMENT OF HEAD AND NECK CANCER WITH INTENSITY MODULATED RADIOTHERAPY

E. BRIAN BUTLER, M.D.,* BIN S. TEH, M.D.,* WALTER H. GRANT, III, PH.D.,* BARRY M. UHL, M.D.,* RONALD B. KUPPERSMITH, M.D.,† J. KAM CHIU, M.D.,* DONALD T. DONOVAN, M.D.,† AND SHIAO Y. WOO, M.D.*

2000 — **Considerazioni radiobiologiche**

Int. J. Radiation Oncology Biol. Phys., Vol. 46, No. 3, pp. 619–630, 2000
Copyright © 2000 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/00/$–see front matter
PII S0360-3016(99)00438-1

BIOLOGY CONTRIBUTION

RADIOBIOLOGICAL CONSIDERATIONS IN THE DESIGN OF FRACTIONATION STRATEGIES FOR INTENSITY-MODULATED RADIATION THERAPY OF HEAD AND NECK CANCERS

RADHE MOHAN, PH.D.,* QIUWEN WU, PH.D.,* MATTHEW MANNING, M.D.,* AND RUPERT SCHMIDT-ULLRICH, M.D.*

*Department of Radiation Oncology, Medical College of Virginia, Virginia Commonwealth University and McGuire VA Hospital, Richmond, VA

2000 — **Risultati dei primi studi clinici**

Int. J. Radiation Oncology Biol. Phys., Vol. 49, No. 4, pp. 907–916, 2001
Copyright © 2001 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/01/$–see front matter
PII S0360-3016(00)01441-3

CLINICAL INVESTIGATION — Head and Neck

A PROSPECTIVE STUDY OF SALIVARY FUNCTION SPARING IN PATIENTS WITH HEAD-AND-NECK CANCERS RECEIVING INTENSITY-MODULATED OR THREE-DIMENSIONAL RADIATION THERAPY: INITIAL RESULTS

K. S. CLIFFORD CHAO, M.D., JOSEPH O. DEASY, PH.D., JERRY MARKMAN, D.SC., JOYCE HAYNIE, R.N., CARLOS A. PEREZ, M.D., JAMES A. PURDY, PH.D., AND DANIEL A. LOW, PH.D.

2001 — **Prime raccomandazioni/linee guida**

Int. J. Radiation Oncology Biol. Phys., Vol. 51, No. 4, pp. 880–914, 2001
Copyright © 2001 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/01/$–see front matter
PII S0360-3016(01)01749-7

CRITICAL REVIEW

INTENSITY-MODULATED RADIOTHERAPY: CURRENT STATUS AND ISSUES OF INTEREST

Intensity Modulated Radiation Therapy Collaborative Working Group

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

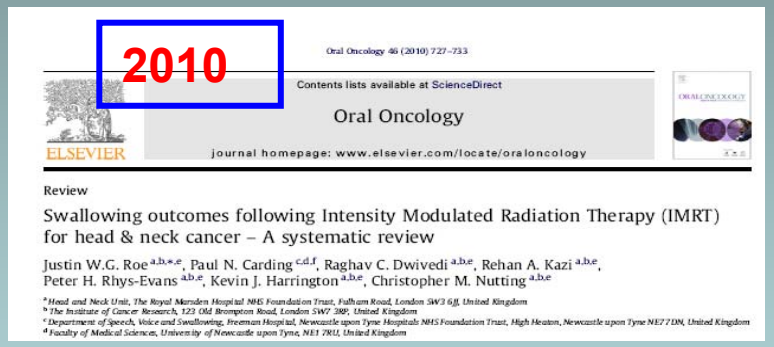
Incontro AIRO - AIFM Lombardia

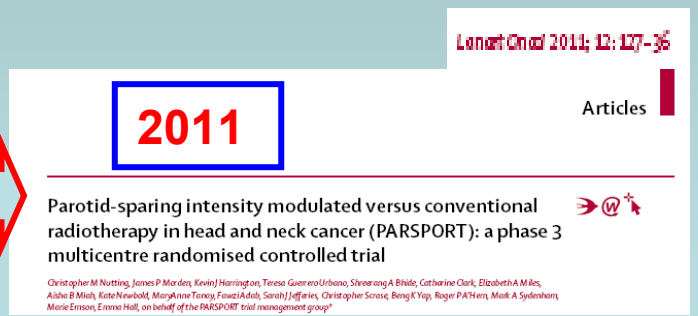
IMRT IN HEAD & NECK CANCER

IL PRESENTE: PROMISE FULFILLED?

"Consacrazione" dell'IMRT con le raccomandazioni ICRU 83

Reviews sistematiche sulla qualità di vita dopo IMRT per H&N Cancer





Risultati dello studio randomizzato multicentrico PARSPORT: "largest randomised trial of IMRT in H & N Cancer"…

…Ma ci dono ancora molti interrogativi…

Worthwhile quality of life gain?

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

Evoluzione negli ultimi 10 anni…

CONFRONTO IMRT/3DCRT: "parotid sparing & dose escalation"

Int. J. Radiation Oncology Biol. Phys., Vol. 48, No. 2, pp. 329–337, 2000
Copyright © 2000 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/00/$–see front matter

ELSEVIER

2000

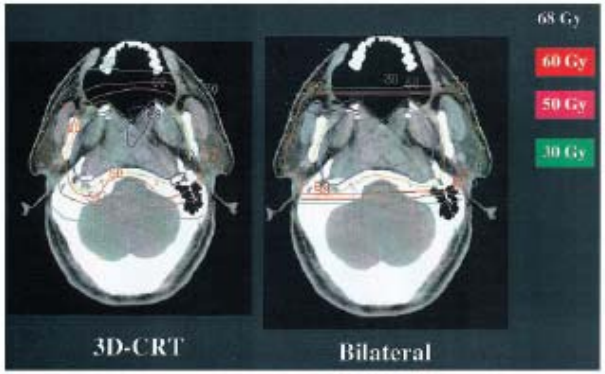
PII S0360-3016(00)00585-X

CLINICAL INVESTIGATION — **Head and Neck**

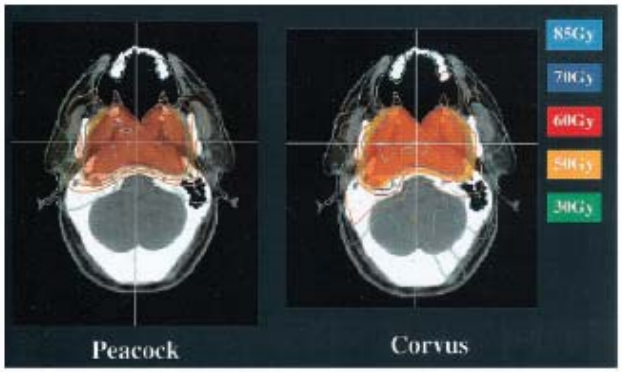
COMPARISON OF TREATMENT PLANS INVOLVING INTENSITY-MODULATED RADIOTHERAPY FOR NASOPHARYNGEAL CARCINOMA

PING XIA, PH.D., KAREN K. FU, M.D., GORDON W. WONG, B.S., CLAYTON AKAZAWA, C.M.D., AND LYNN J. VERHEY, PH.D.

Department of Radiation Oncology, University of California at San Francisco, San Francisco, CA



(a)



(a)

Int. J. Radiation Oncology Biol. Phys., Vol. 46, No. 1, pp. 195–205, 2000
Copyright © 2000 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/00/$–see front matter

ELSEVIER

2000

PII S0360-3016(99)00304-1

PHYSICS CONTRIBUTION

THE POTENTIAL FOR SPARING OF PAROTIDS AND ESCALATION OF BIOLOGICALLY EFFECTIVE DOSE WITH INTENSITY-MODULATED RADIATION TREATMENTS OF HEAD AND NECK CANCERS: A TREATMENT DESIGN STUDY

QIUWEN WU, PH.D., MATTHEW MANNING, M.D., RUPERT SCHMIDT-ULLRICH, M.D., AND RADHE MOHAN, PH.D.

Department of Radiation Oncology, Medical College of Virginia, Virginia Commonwealth University and McGuire VA Hospital, Richmond, VA

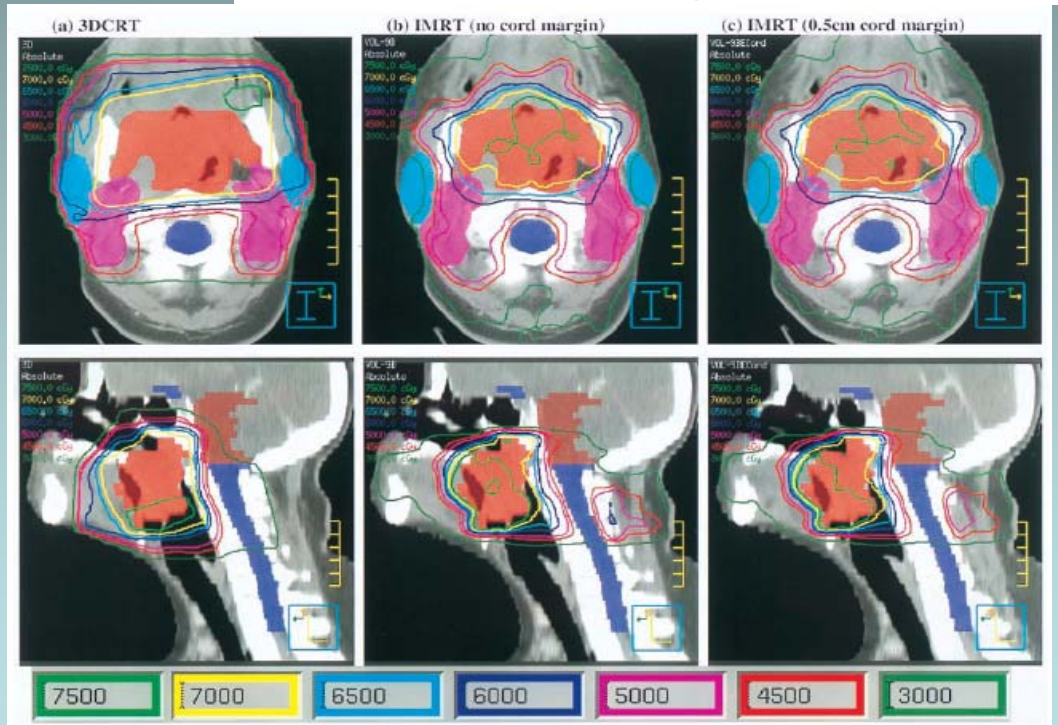


Fig. 1. Transverse and sagittal views of dose distributions comparing (a) the standard 3DCRT plan with (b) an IMRT plan and (c) another IMRT plan, in which a margin of 0.5 cm around the cord has been added. All plans are for 4 MV. The IMRT plans employed nine coplanar, noncollinear beams placed at equiangular steps. The IMRT optimization criteria was dose-volume based.

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

CONFRONTO TRA DVH: IMRT "more conformal, higher OARs sparing"

Verifica dei moduli IMRT nei diversi TPS

2003

ELSEVIER
Radiotherapy and Oncology 66 (2003) 29–40
RADIOTHERAPY & ONCOLOGY
www.elsevier.com/locate/radonline

Comparative analysis of intensity modulation inverse planning modules of three commercial treatment planning systems applied to head and neck tumour model

Antonella Fogliata[a,*], Alessandra Bolsi[a,b], Luca Cozzi[a]

[a]Oncology Institute of Southern Switzerland, Medical Physics Unit, Radiation Oncology Department, Bellinzona, Switzerland
[b]University of Milan, Medical Physics Specialisation School, Milan, Italy

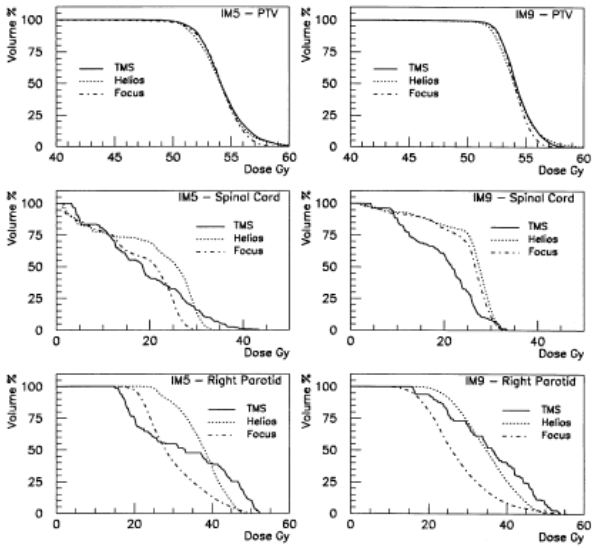


Fig. 3. Example DVHs for PTV, spinal cord, and right parotid, resulting from the second complexity level, according to IM5 and IM9.

2004

ELSEVIER
Int. J. Radiation Oncology Biol. Phys., Vol. 58, No. 2, pp. 617–624, 2004
Copyright © 2004 Elsevier Inc.
Printed in the USA. All rights reserved
0360-3016/04/$–see front matter
doi:10.1016/j.ijrobp.2003.09.059

Analisi delle distribuzioni di dose IMRT vs 3DCRT

ICTR 2003 Translational Research in Clinics

THREE-DIMENSIONAL CONFORMAL VS. INTENSITY-MODULATED RADIOTHERAPY IN HEAD-AND-NECK CANCER PATIENTS: COMPARATIVE ANALYSIS OF DOSIMETRIC AND TECHNICAL PARAMETERS

Luca Cozzi, Ph.D.,* Antonella Fogliata, Dr.,* Alessandra Bolsi, Dr.,*†
Giorgia Nicolini, Dr.,* and Jacques Bernier, Ph.D., M.D.‡

*Medical Physics Unit and ‡Department of Radiation Oncology, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; †Medical Physics School, University of Milan, Milan, Italy

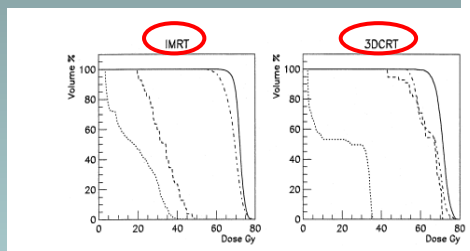


Fig. 2. Cumulative dose–volume histograms for target volumes and organs at risk for the same representative patient. Data are shown for the whole treatment with IMRT (70.2 Gy) or for the reference 3DCRT technique. The solid line represents PTVI, the dashed-dotted line represents PTVII–PTVI, the dashed line represents the parotid gland, and the dotted line represents the spinal cord.

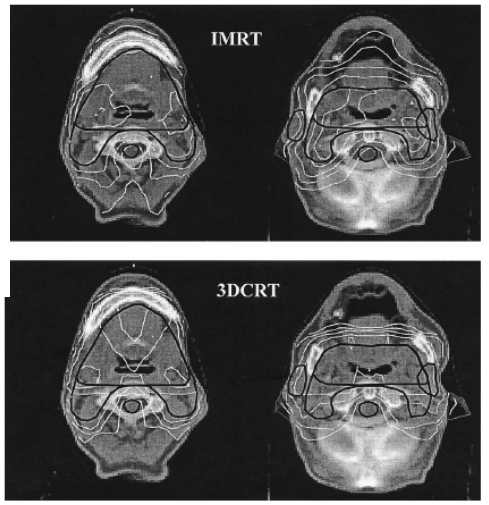


Fig. 1. Isodose distributions at (a) isocenter level and at (b) parotids level for 1 representative patient (Patient 7 in Table 1). Curves are shown for whole treatment (total dose: 70.2 Gy) with IMRT and for the reference 3DCRT technique. Isodose lines represent 36, 45, 54, 65, and 72 Gy, which correspond to, respectively, 50%, 62%, 75%, 90%, and 100%.

EVIDENTE SUPERIORITA' DELLE DISTRIBUZIONI DI DOSE AGLI OARs con IMRT vs 3DCRT

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

VERIFICA DELLA PRECISIONE DI CONTOURING E DELIVERY

La maggior parte delle recidive si manifesta nel CTV1 (volume di alta dose): "target definition and coverage is adequate for IMRT"

Int. J. Radiation Oncology Biol. Phys., Vol. 55, No. 2, pp. 312–321, 2003
Copyright © 2003 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/03/$–see front matter
PII S0360-3016(02)03940-8

2003

Primi dati sulle sedi di ricaduta

CLINICAL INVESTIGATION — Head and Neck

PATTERNS OF FAILURE IN PATIENTS RECEIVING DEFINITIVE AND POSTOPERATIVE IMRT FOR HEAD-AND-NECK CANCER

K. S. Clifford Chao, M.D.,* Gokhan Ozyigit, M.D.,* Binh N. Tran, M.D.,* Mustafa Cengiz, M.D.,* James F. Dempsey, Ph.D.,† and Daniel A. Low, Ph.D.*

*Department of Radiation Oncology, Washington University Medical School, St. Louis, MO; †Department of Radiation Oncology, University of Florida, Gainesville, FL

Table 2. AJCC stage distribution of 126 patients

	Tx	T1	T2	T3	T4	Total
N0	—	5	7	7	11	30
N1	1	4	10	4	7	26
N2	7	10	14	13	17	61
N3	1	—	2	3	3	9
Total	9	19	33	27	38	126

AJCC stage	Overall (n = 117)*	Definitive IMRT (n = 52)	Postoperative IMRT (n = 65)
I	5 (3)	—	5
II	8 (7)	4	4
III	26 (23)	9	17
IV	78 (67)	39	39

Tumori localmente avanzati; IMRT definitiva/postoperatoria

I. J. Radiation Oncology ● Biology ● Physics Volume 55, Number 2, 2003

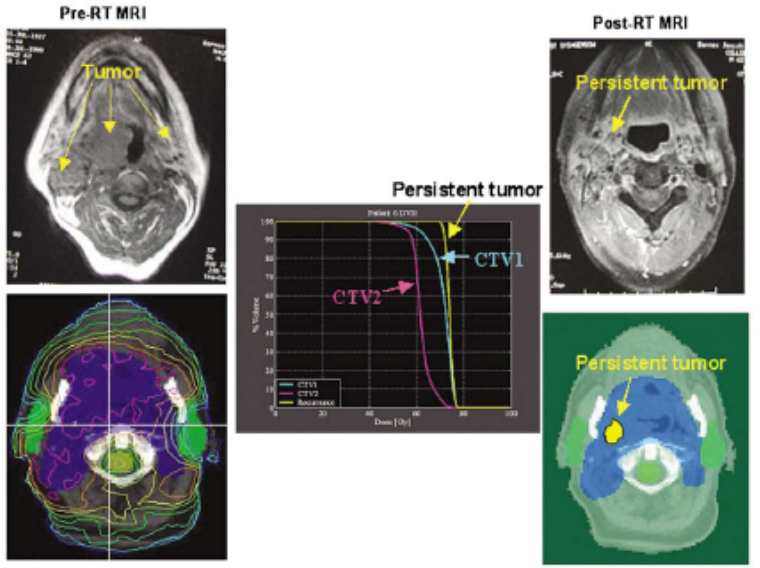


Fig. 2. DVH analysis of persistent tumor in a patient with T3N2b squamous cell carcinoma of the right tonsil receiving definitive IMRT. Location of persistent disease assessed as in-field to CTV1.

Table 4. IMRT clinical target volume and normal tissue dose specification with biological equivalent dose correction for head-and-neck cancer—Washington University guidelines

		IMRT		
Target volume	Conventional technique	Definitive (35 fractions)	High-risk postoperative (33 fractions)	Intermediate-risk postoperative (30 fractions)
CTV1	66–70/2 Gy	70/2 Gy	66/2 Gy	60/2 Gy
CTV2	50–54/2 Gy	56/1.66 Gy	54/1.64 Gy	52/1.73 Gy

Abbreviations as in Table 3.
Normal tissue tolerance for IMRT prescription: Optic nerve and optic chiasm 55 Gy, retina 45 Gy, brainstem 50–55 Gy, spinal cord 45–48 Gy, parotid gland 20–30 Gy, mandible 70 Gy.

Utile dose escalation

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

OUTCOMES COMPARABILI CON 2DRT E 3DCRT

PRIMI DATI CLINICI

RETROSPETTIVI

2003

Int. J. Radiation Oncology Biol. Phys., Vol. 55, No. 2, pp. 312–321, 2003
Copyright © 2003 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/03/$–see front matter
PII S0360-3016(02)03940-8

CLINICAL INVESTIGATION — Head and Neck

PATTERNS OF FAILURE IN PATIENTS RECEIVING DEFINITIVE AND POSTOPERATIVE IMRT FOR HEAD-AND-NECK CANCER

K. S. Clifford Chao, M.D.,* Gokhan Ozyigit, M.D.,* Binh N. Tran, M.D.,* Mustafa Cengiz, M.D.,* James F. Dempsey, Ph.D.,† and Daniel A. Low, Ph.D.*

*Department of Radiation Oncology, Washington University Medical School, St. Louis, MO; †Department of Radiation Oncology, University of Florida, Gainesville, FL

Table 7. Head-and-neck IMRT results

	Locoregional failures	2-y Actuarial locoregional control rate (%)	2-y Ultimate actuarial locoregional control rate*
Overall	17/126 (13)	85	89
Definitive IMRT	10/52 (19)	79	84
Postoperative IMRT	7/74 (9)	90	93

Abbreviation: IMRT = intensity-modulated radiotherapy.
* After salvage surgery.

I vantaggi dosimetrici della IMRTsi traducono in significative riduzioni della tossicità salivare senza impatto negativo su LC e DFS sia per RT definitiva sia in postoperatoria

2001

ELSEVIER
Radiotherapy and Oncology 61 (2001) 275–280
RADIOTHERAPY & ONCOLOGY
www.elsevier.com/locate/radonline

Intensity-modulated radiation therapy reduces late salivary toxicity without compromising tumor control in patients with oropharyngeal carcinoma: a comparison with conventional techniques

K.S. Clifford Chao[a,*], Navneet Majhail[a], Chih-jen Huang[a], Joseph R. Simpson[a], Carlos A. Perez[a], Bruce Haughey[b], Gershon Spector[b]

[a]Department of Radiation Oncology, Washington University Medical Center, St. Louis, MO, USA
[b]Department of Otolaryngology, Washington University Medical Center, St. Louis, MO, USA

Table 3
Moderate to severe acute complications[a]

ACUTE REACTIONS

	Preoperative CRT (n = 109)	Postoperative CRT (n = 142)	Definitive CRT (n = 153)	Postoperative IMRT (n = 14)	Definitive IMRT (n = 12)
Skin					
Grade 2	30 (28)	78 (56)	99 (65)	5 (36)	4 (34)
Grade 3	0 (0)	4 (3)	12 (8)	3 (21)	3 (25)
Mucosa					
Grade 2	39 (36)	85 (60)	102 (67)	10 (71)	7 (58)
Grade 3	0 (0)	28 (20)	38 (25)	3 (21)	5 (42)
Salivary gland					
> Grade 2	20 (19)	90 (65)	106 (79)	9 (64)	9 (75)
Pharynx					
Grade 2	33 (30)	48 (34)	73 (48)	3 (22)	3 (25)
Grade 3	2 (2)	24 (17)	28 (18)	1 (7)	3 (25)
Loss of weight (>10%)	2 (2)	21 (15)	26 (17)	0 (0)	3 (25)
G-tube required[b]	2 (2)	24 (17)	28 (18)	1 (7)	3 (25)

[a] Figures in parentheses represent percentage values.
[b] Gastrostomy tube (G-tube) insertion required due to chemotherapy or radiation therapy.

In conclusion, when IMRT was compared with conventional techniques, the dosimetric advantage of IMRT did translate into a significant reduction of late salivary toxicity in patients with oropharyngeal carcinoma. No adverse impact on tumor control and disease-free survival was observed in patients treated with IMRT.

Table 4
Moderate to severe late complications[a,b]

LATE REACTIONS

	Preoperative CRT (n = 101)	Postoperative CRT (n = 139)	Definitive CRT (n = 143)	Postoperative IMRT (n = 12)	Definitive IMRT (n = 10)
Skin					
Grade 2	5 (5)	21 (15)	24 (17)	1 (8)	1 (10)
Grade 3	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Mucosa					
Grade 2	2 (2)	24 (18)	17 (12)	0 (0)	1 (10)
Grade 3	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Salivary gland					
Grade 2	32 (32)	107 (75)	114 (80)	2 (17)	3 (30)
Grade 3	0 (0)	3 (2)	6 (4)	0 (0)	0 (0)
Trismus	3 (3)	3 (2)	3 (2)	1 (8)	0 (0)
Osteoradionecrosis	6 (6)	4 (3)	9 (7)	0 (0)	0 (0)
Soft tissue necrosis	2 (2)	1 (1)	1 (1)	0 (0)	0 (0)

[a] Excluding patients with persistent or recurrent disease.
[b] Figures in parentheses represent percentage values.

Table 2
Local–regional control, disease-free and overall survival of the study population

LRC & DFS

	Preoperative CRT (n = 109)	Postoperative CRT (n = 142)	Definitive CRT (n = 153)	Postoperative IMRT (n = 14)	Definitive IMRT (n = 12)
Follow-up (years)[a]	4.5 (1.5–23)	3.9 (1.3–19.8)	3.5 (1.6–17.7)	2.2 (1–3.2)	2 (1–2.8)
Two-year local–regional control (%)	78	76	68	100	88
Two-year disease-free survival (%)	68	74	58	92	80
Two-year overall survival (%)	67	71	57	100	100

[a] Figures in parentheses represent ranges.

HUMANITAS GAVAZZENI

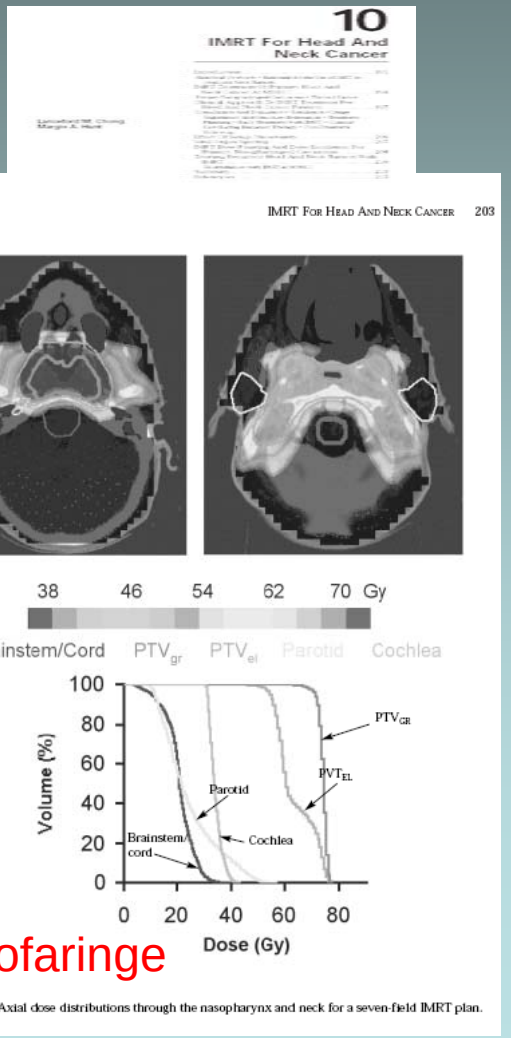
Sabato 21 MAGGIO 2011

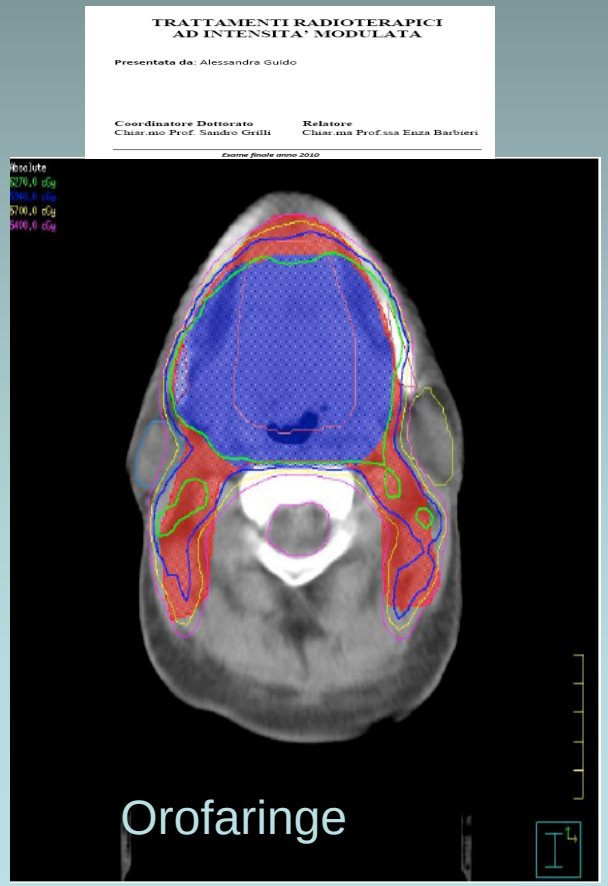
Incontro AIRO - AIFM Lombardia

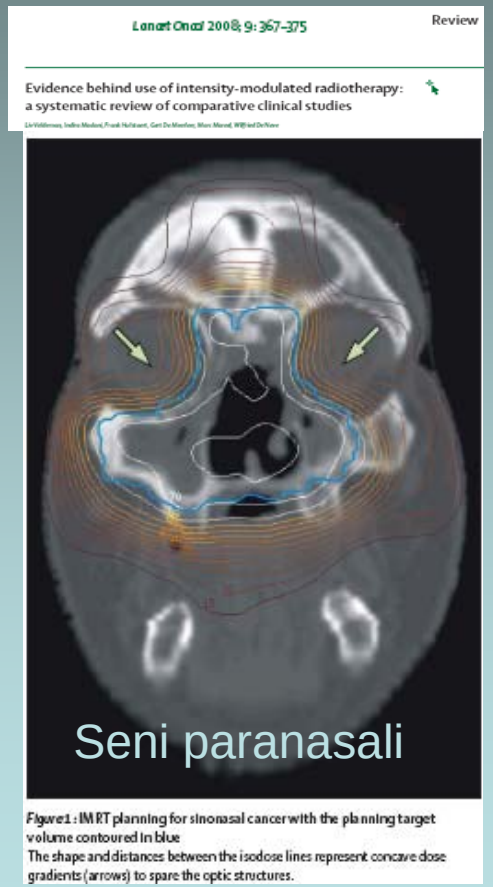
IMRT IN HEAD & NECK CANCER

Vantaggi dosimetrici della IMRT…

CONFERMA DELLA CAPACITA' DI RIDURRE LA DOSE A VARI OARs IN DIFFERENTI SEDI DEL DISTRETTO HEAD & NECK







HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

Dalla dosimetria alla clinica…

STUDI CLINICI CON IMRT IN DIFFERENTI SEDI HEAD & NECK

Clin Transl Oncol (2008) 10:407-414
DOI 10.1007/s12094-008-0224-7

REVIEWS

Clinical application of intensity-modulated radiotherapy for head and neck cancer

Olivier Ballivy · Ramón Galiana Santamaría · Alicia Lozano Borbalas · Ferrán Guedea Edo

VALUTAZIONI DI OUTCOME

2002-2007

Table 1 Clinical series of intensity-modulated radiotherapy (IMRT) for head and neck cancer

Series	No.	Tumor sites	Definitive/ adjuvant	Stage III–IV	Chemotherapy	Follow-up	LRCR, LCR/RCR	Overall survival
Chao et al [11] 2002	126	Oropharynx (63), oral cavity (15), nasopharynx (12), nasal/sinus (9), larynx (8), hypopharynx (8), unknown primary (9)	52/74	90%	32%	26 months	85% (2 years)	–
Lee et al [12] 2003	150	Nasopharynx (86), oropharynx (22), nasal/sinus (24), thyroid (6), others (12)	107/43	82%	72%	21 months	87% (3 years)	84% (3 years)
Yao et al [13] 2004	150	Oropharynx (56), larynx (33), oral cavity (29), hypopharynx (8), nasal/sinus (8), nasopharynx (5), unknown (11)	99/51	85%	45%	18 months	92% (2 years)	85% (2 years)
Feng et al [14] 2005	158	Oropharynx (94), oral cavity (36), hypopharynx (13), larynx (12), unknown primary (3)	72/86	80%	43%	36 months	85% (2 years)	84% (2 years)
Studer et al [15] 2006	115	Oropharynx (56), oral cavity (19), hypopharynx (16), nasal/sinus (12), larynx (7)	80/34	62%	77%	18 months	77% LC (2 years)	88% (2 years)
Kwong et al [16] 2003	50	Nasopharynx	Definitive IMRT only	T1-2/N0-1	0	14 months	100/94% (3 years)	100% (3 years)
Kam et al [17] 2004	63	Nasopharynx	Definitive IMRT only	57%	30%	29 months	92/98% (3 years)	90% (3 years)
Wolden et al [18] 2006	74	Nasopharynx	Definitive IMRT only	77%	93%	35 months	91/93% (3 years)	83% (3 years)
de Arruda et al [19] 2005	50	Oropharynx	48/2	92% (34% T3-4)	86%	18 months	98/88% (2 years)	98% (2 years)
Garden et al [20] 2007	51	Oropharynx	Definitive IMRT only	71% (T1-2 only)	10%	45 months	96/94% (2 years)	94% (2 years)
Hodge et al [21] 2007	52	Oropharynx	Definitive IMRT only	86% (13% T3-4)	54%	24 months	96% (3 years)	88% (3 years)

No. patient number, *LRCR* locoregional tumor control rate, *LCR/RCR* local control rate/regional control rate

***STUDI DI FATTIBILITA'(SERIE RETROSPETTIVE)**

***DIFFERENTI FINALITA' DEL TRATTAMENTO: DEFINITIVO/POSTOP.**

***VARIE ASSOCIAZIONI CON CHT**

***ENDPOINTS: LC/LRC/OS**

CONCLUSIONI: "…sparing the parotid glands with IMRT can be achieved without compromising treatment outcome…"

The encouraging locoregional tumor control rate reported in these series suggests that sparing the parotids glands with IMRT can be achieved without compromising treatment outcome. For nasopharyngeal and oropharyngeal cancers, the tumor control rate with IMRT compares favorably to that achieved with conventional RT. In a recent

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

STUDI CLINICI DI IMRT SULLA RIDUZIONE DELLA XEROSTOMIA E SULLA QUALITA' DI VITA

VALUTAZIONI DI FUNZIONE D'ORGANO E QOL

Clin Transl Oncol (2008) 10:407-414
DOI 10.1007/s12094-008-0224-7

REVIEWS

Clinical application of intensity-modulated radiotherapy for head and neck cancer

Olivier Ballivy · Ramón Galiana Santamaría · Alicia Lozano Borbalas · Ferrán Guedea Edo

2005-2007

Table 2 Clinical investigations of xerostomia and quality of life (QOL) for head and neck cancer patients treated with intensity-modulated radiotherapy (IMRT) *vs.* radiotherapy (RT)

Study	No. (IMRT/CRT)	Design	Parotid mean dose	Xerostomia/QOL instruments	Conclusions
Jabbari et al [24] 2005	40 (30/10)	Matched case-control 3:1 (age, site stage)	IMRT < 26 Gy CRT > 50 Gy	HNQOL & XQ	Median XQ and HNQOL score were better in IMRT
Braam et al [25] 2006	56 (30/26)	Prospective evaluation nonrandomized comparison	IMRT 30 Gy CRT 48,7 Gy	Salivary flow measurement (at 6 months)	Significant improvement in salivary flow (> 25% of baseline) with IMRT (44%) vs. CRT (19%)
Fang et al [26] 2006	237 (85/152)	Retrospective comparison	–	EORTC QLQ C-30 and H&N35	Significant improvement in global/H&N QLQ score with IMRT
Graff et al [27] 2007	134 (67/67)	Matched pair comparison (T stage, delay since end of RT)	IMRT 33 Gy	EORTC QLQ C-30 and H&N35	Better H&N QLQ score for IMRT and prevalence odds ratio for dry mouth in favor of IMRT (3.17)
Lee et al [28]	99 (41/55)	Retrospective comparison	IMRT < 26 Gy (planning goal)	RTOG toxicity xerostomia score	Grade 2-3 xerostomia significantly less with IMRT (62%) *vs.* CRT (67%)
Pow et al [29] 2007	46 (24/21)	Prospective phase III (randomized)	IMRT 41 Gy	EORTC QLQ C-30 and H&N35 & Salivary flow (12 months)	Xerostomia related symptoms significantly less with IMRT Salivary flow > 25% baseline in 83% with IMRT vs. 10% CRT
Yao et al [30] 2007	55 (26/27)	Retrospective comparison	–	HRQOL H&N cancer inventory	Higher QOL score for each of the 4 H&N domains with IMRT

N patient number, *CRT* conventional radiotherapy, *EORTC QLQ H&N 35* European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire C30 and Head and Neck Cancer Module, *HNQOL* Head and Neck QOL questionnaire, *XQ* xerostomia questionnaire, *HRQOL* Health-related QOL surveys, *LRCR* locoregional tumor control rate, *LCR/RCR* local control rate/regional control rate

***NOTEVOLI DIFFERENZE NEL DISEGNO DEGLI STUDI (RETROSPETTICO, RANDOMIZZATO, CASO-CONTROLLO, PROSPETTICO NON RANDOMIZZATO)**

***SIGNIFICATIVA VARIABILITA'NEGLI ENDPOINTS CLINICI UTILIZZATI PER VALUTARE LA FUNZIONE SALIVARE**

…TUTTAVIA: "…the majority of these publications suggest that parotid-sparing IMRT is successful in reducing posttreatment salivary toxicity…"

with IMRT [24–30] (Table 2). Despite significant variability in the study design and the clinical endpoints used to assess salivary function, the majority of these publications suggest that parotid-sparing IMRT is successful in reducing posttreatment salivary toxicity.

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

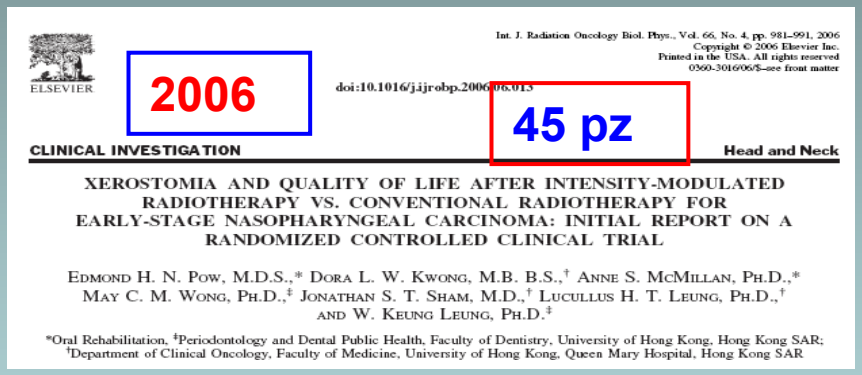
Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

Evidence based IMRT?...

STUDI RANDOMIZZATI IMRT VS 3DCRT IN HEAD & NECK CANCER

La IMRT è stata confrontata con la 2D/3DCRT in 3 studi randomizzati pubblicati: 2 nei tumori della rinofaringe ed 1, recentissimo, in tumori dell'orofaringe ed ipofaringe



Int. J. Radiation Oncology Biol. Phys., Vol. 66, No. 4, pp. 981–991, 2006
Copyright © 2006 Elsevier Inc.
Printed in the USA. All rights reserved
0360-3016/06/$–see front matter

ELSEVIER

2006

doi:10.1016/j.ijrobp.2006.06.013

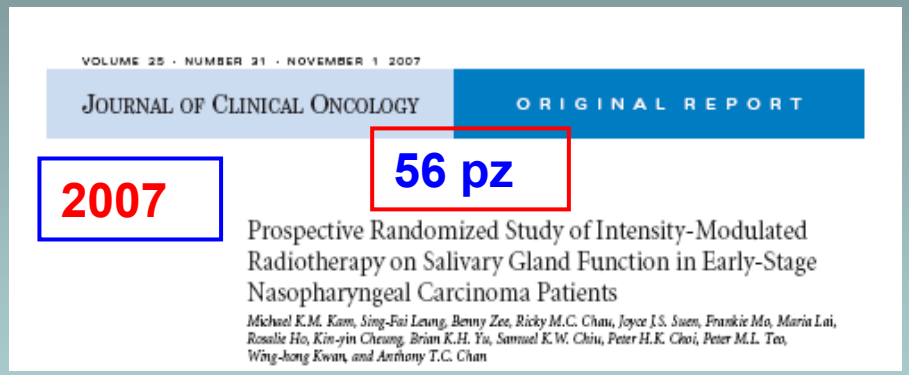
45 pz

CLINICAL INVESTIGATION — Head and Neck

XEROSTOMIA AND QUALITY OF LIFE AFTER INTENSITY-MODULATED RADIOTHERAPY VS. CONVENTIONAL RADIOTHERAPY FOR EARLY-STAGE NASOPHARYNGEAL CARCINOMA: INITIAL REPORT ON A RANDOMIZED CONTROLLED CLINICAL TRIAL

EDMOND H. N. POW, M.D.S.,* DORA L. W. KWONG, M.B. B.S.,† ANNE S. MCMILLAN, PH.D.,* MAY C. M. WONG, PH.D.,‡ JONATHAN S. T. SHAM, M.D.,† LUCULLUS H. T. LEUNG, PH.D.,† AND W. KEUNG LEUNG, PH.D.‡

*Oral Rehabilitation, ‡Periodontology and Dental Public Health, Faculty of Dentistry, University of Hong Kong, Hong Kong SAR; †Department of Clinical Oncology, Faculty of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong SAR



VOLUME 25 · NUMBER 31 · NOVEMBER 1 2007

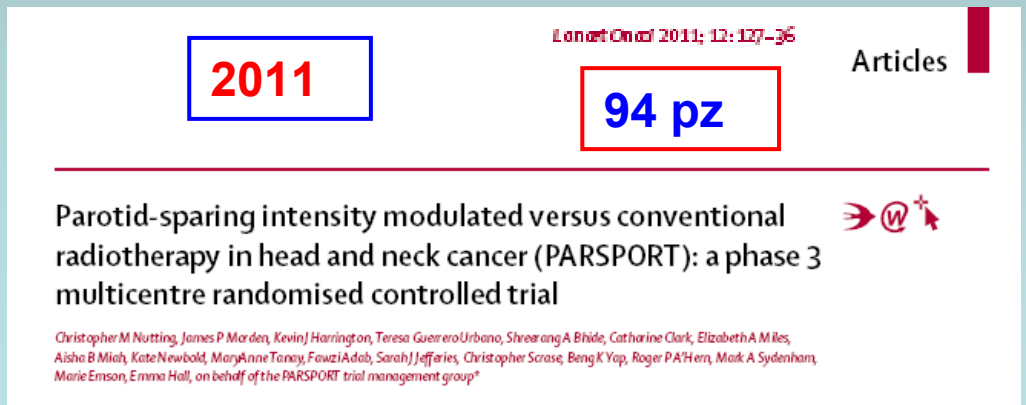
JOURNAL OF CLINICAL ONCOLOGY — ORIGINAL REPORT

2007

56 pz

Prospective Randomized Study of Intensity-Modulated Radiotherapy on Salivary Gland Function in Early-Stage Nasopharyngeal Carcinoma Patients

Michael K.M. Kam, Sing-Fai Leung, Benny Zee, Ricky M.C. Chau, Joyce L.S. Suen, Frankie Mo, Maria Lai, Rosalie Ho, Kin-yin Cheung, Brian K.H. Yu, Samuel K.W. Chiu, Peter H.K. Choi, Peter M.L. Teo, Wing-hong Kwan, and Anthony T.C. Chan



Lancet Oncol 2011; 12: 127–36

Articles

2011

94 pz

Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

*Christopher M Nutting, James P Morden, Kevin J Harrington, Teresa Guerrero Urbano, Shreerang A Bhide, Catharine Clark, Elizabeth A Miles, Aisha B Miah, Kate Newbold, MaryAnne Tanay, Fawzi Adab, Sarah J Jefferies, Christopher Scrase, Beng K Yap, Roger P A'Hern, Mark A Sydenham, Marie Emson, Emma Hall, on behalf of the PARSPORT trial management group**

HUMANITAS GAVAZZENI

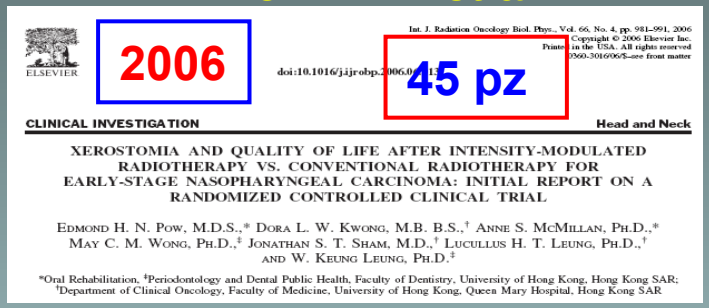
Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

STUDI RANDOMIZZATI

Pow EHN et al



ELSEVIER

2006

Int. J. Radiation Oncology Biol. Phys., Vol. 66, No. 4, pp. 981–991, 2006
Copyright © 2006 Elsevier Inc.
Printed in the USA. All rights reserved
0360-3016/06/$–see front matter
doi:10.1016/j.ijrobp.2006.01.013

45 pz

CLINICAL INVESTIGATION — Head and Neck

XEROSTOMIA AND QUALITY OF LIFE AFTER INTENSITY-MODULATED RADIOTHERAPY VS. CONVENTIONAL RADIOTHERAPY FOR EARLY-STAGE NASOPHARYNGEAL CARCINOMA: INITIAL REPORT ON A RANDOMIZED CONTROLLED CLINICAL TRIAL

EDMOND H. N. POW, M.D.S.,* DORA L. W. KWONG, M.B. B.S.,† ANNE S. MCMILLAN, PH.D.,* MAY C. M. WONG, PH.D.,‡ JONATHAN S. T. SHAM, M.D.,† LUCULLUS H. T. LEUNG, PH.D.,† AND W. KEUNG LEUNG, PH.D.‡

*Oral Rehabilitation, ‡Periodontology and Dental Public Health, Faculty of Dentistry, University of Hong Kong, Hong Kong SAR; †Department of Clinical Oncology, Faculty of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong SAR

NPC: T2 N0/N1 M0 (Stage II AJCC 1997)

IMRT: 24 pts; 3DCRT: 21 pts

PRIMARY ENDPOINT VARIABLE: CHANGE IN STIMULATED WHOLE SALIVARY FLOW RATE

QOL EVALUATION: SF-36, EORTC QOL H&N35

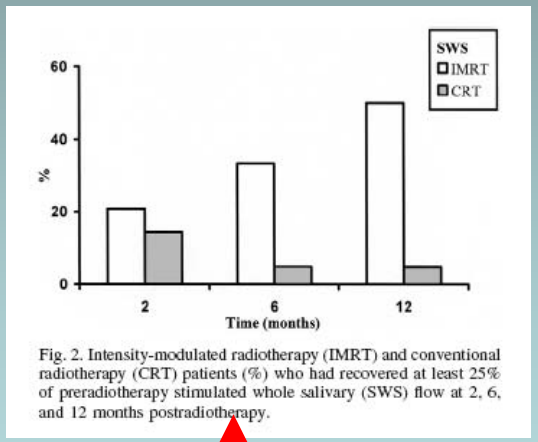


Fig. 2. Intensity-modulated radiotherapy (IMRT) and conventional radiotherapy (CRT) patients (%) who had recovered at least 25% of preradiotherapy stimulated whole salivary (SWS) flow at 2, 6, and 12 months postradiotherapy.

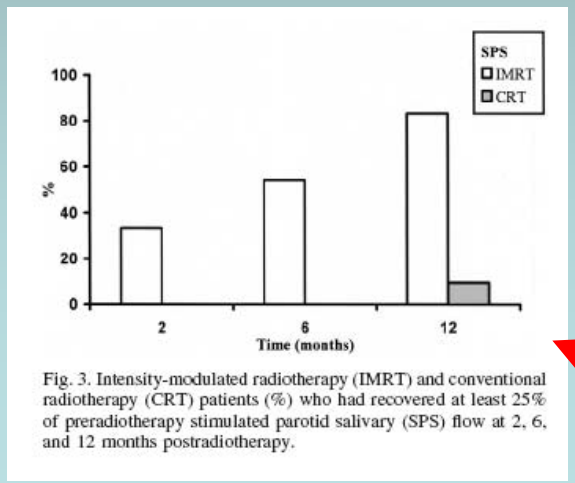


Fig. 3. Intensity-modulated radiotherapy (IMRT) and conventional radiotherapy (CRT) patients (%) who had recovered at least 25% of preradiotherapy stimulated parotid salivary (SPS) flow at 2, 6, and 12 months postradiotherapy.

CONCLUSIONI: "…IMRT significantly better in terms of parotid sparing and improved QOL…"

IMRT: miglior recupero flusso salivare totale stimolato a 2, 6, 12 mesi post RT

IMRT: miglior recupero flusso salivare parotideo stimolato a 2, 6, 12 mesi post RT

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

STUDI RANDOMIZZATI

Kam MKM et al

VOLUME 25 · NUMBER 31 · NOVEMBER 1 2007

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

2007

56 pz

Prospective Randomized Study of Intensity-Modulated Radiotherapy on Salivary Gland Function in Early-Stage Nasopharyngeal Carcinoma Patients

Michael K.M. Kam, Sing-Fai Leung, Benny Zee, Ricky M.C. Chau, Joyce J.S. Suen, Frankie Mo, Maria Lai, Rosalie Ho, Kin-yin Cheung, Brian K.H. Yu, Samuel K.W. Chiu, Peter H.K. Choi, Peter M.L. Teo, Wing-hong Kwan, and Anthony T.C. Chan

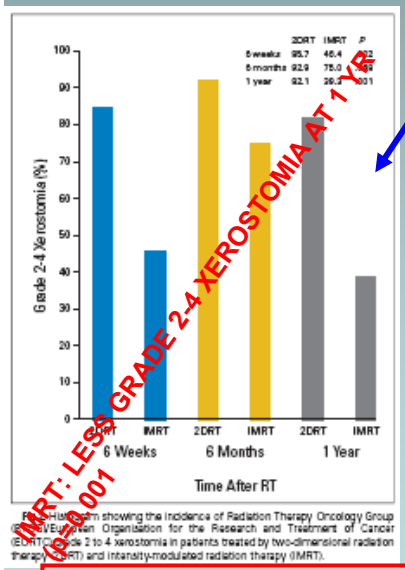
NPC: T1-2b N0/N1 M0 (AJCC 1997)

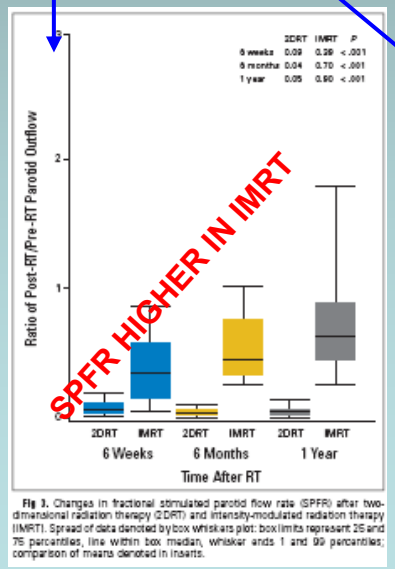
IMRT: 28 pts; 2DRT: 28 pts

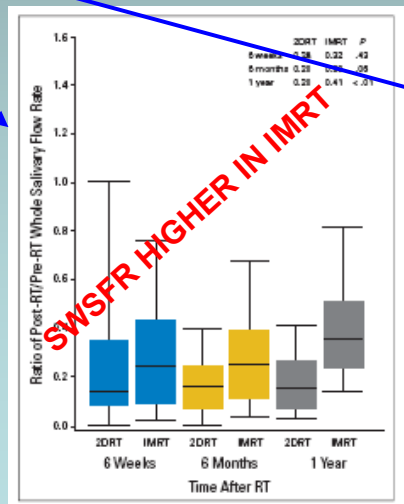
PRIMARY ENDPOINT: INCIDENCE OF OBSERVER-RATED XEROSTOMIA AT 1 YEAR (RTOG/EORTC)

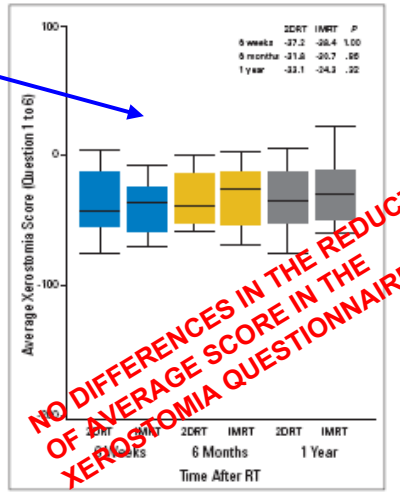
PARALLEL ASSESSMENT WITH PATIENT-REPORTED OUTCOME, STIMULATED PAROTID FLOW RATE, AND WHOLE SALIVA FLOW RATE (XEROSTOMIA QUESTIONNAIRE)

CONCLUSIONI









Continual recovery of xerostomia beyond the 1st year of IMRT

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

STUDI RANDOMIZZATI

Nutting CM et al (Studio PARSPORT)

2011

94 pz

Articles

Lancet Oncol 2011; 12: 127–36

Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

Christopher M Nutting, James P Morden, Kevin J Harrington, Teresa Guerrero Urbano, Shreerang A Bhide, Catharine Clark, Elizabeth A Miles, Aisha B Miah, Kate Newbold, MaryAnne Tanay, Fawzi Adab, Sarah J Jefferies, Christopher Scrase, Beng K Yap, Roger PA'Hern, Mark A Sydenham, Marie Emson, Emma Hall, on behalf of the PARSPORT trial management group*

OROPHARYNX/HYPOPHARYNX: T1-4 N0-3 M0

IMRT: 47 pts; 3DCRT: 47 pts

PRIMARY ENDPOINT: % OF PTS WITH GRADE 2+ XEROSTOMIA AT 1 YR (LENT SOMA scale)

SECONDARY ENDPOINTS: % OF PTS WITH ANY MEASURABLE SALIVARY FLOW AFTER RT, ACUTE /LATE RT SIDE-EFFECTS, QOL (INCLUDING XEROSTOMIA-RELATED QOL), LRC, PFS, OS

% G2+ LENT SOMA xerostomia

% G2+ RTOG xerostomia

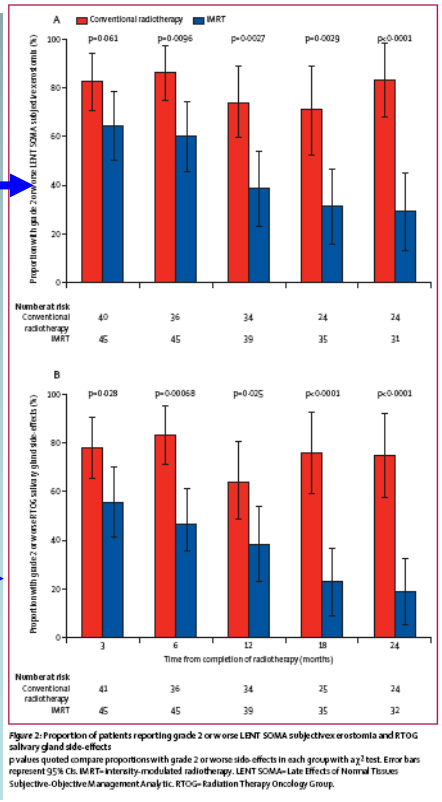


Figure 2: Proportion of patients reporting grade 2 or worse LENT SOMA subjective xerostomia and RTOG salivary gland side-effects

p values quoted compare proportions with grade 2 or worse side-effects in each group with a χ^2 test. Error bars represent 95% CIs. IMRT=intensity-modulated radiotherapy. LENT SOMA=Late Effects of Normal Tissues Subjective-Objective Management Analytic. RTOG=Radiation Therapy Oncology Group.

CONCLUSIONI: % di xerostomia G2+ (LENT SOMA) sempre inferiore in IMRT vs 3DCRT ad ogni osservazione da 3 a 24 mesi (PRIMARY ENDPOINT)

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

STUDI RANDOMIZZATI

Nutting CM et al (Studio PARSPORT)

2011

94 pz

Articles

Lancet Oncol 2011; 12: 127–36

Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

Christopher M Nutting, James P Morden, Kevin J Harrington, Teresa Guerrero Urbano, Shreerang A Bhide, Catharine Clark, Elizabeth A Miles, Aisha B Miah, Kate Newbold, MaryAnne Tanay, Fouzi Adab, Sarah J Jefferies, Christopher Scrase, Beng K Yap, Roger P A'Hern, Mark A Sydenham, Marie Emson, Emma Hall, on behalf of the PARSPORT trial management group*

Concordanza tra flusso salivare non stimolato controlaterale e xerostomia soggettiva G2+ (LENT SOMA scale) a 12 mesi (SECONDARY ENDPOINT)

	Conventional radiotherapy		IMRT	
	No measurable salivary flow* (n=25)	Measurable salivary flow (n=0)	No measurable salivary flow (n=18)	Measurable salivary flow (n=16)
Subjective xerostomia better than grade 2	6 (24%)	0	10 (56%)	12 (75%)
Subjective xerostomia grade 2 or worse	19 (76%)	0	8 (44%)	4 (25%)

Fisher's exact test for association (treatment groups combined) p=0·018. LENT SOMA=Late Effects of Normal Tissues Subjective-Objective Management Analytic. IMRT=intensity-modulated radiotherapy. *Measurable salivary flow was defined as any saliva collected from the Lashley cup apparatus.

Table 3: Concordance between unstimulated contralateral saliva flow and LENT SOMA subjective xerostomia at 12 months

CONCLUSIONI (SECONDARY ENDPOINTS)

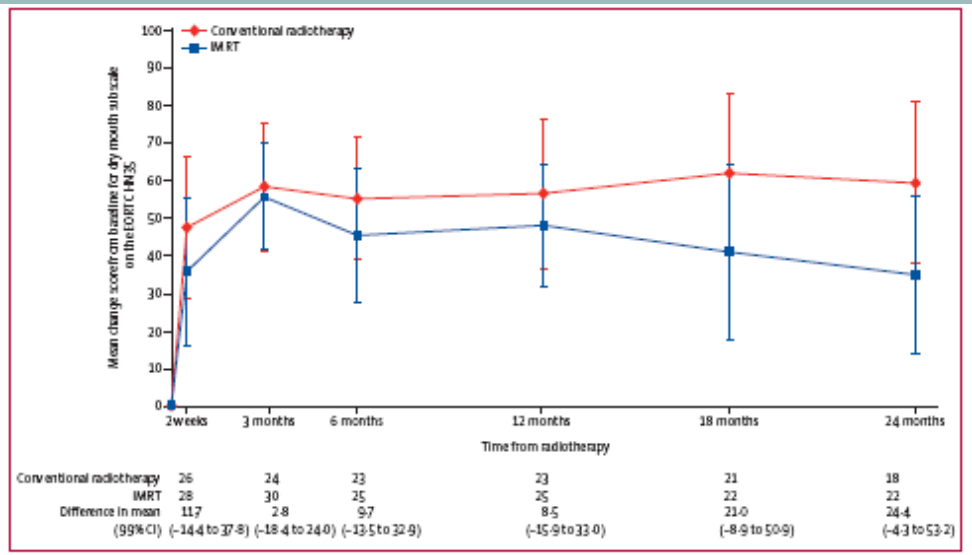


Figure 3: Mean EORTC HN35 dry mouth subscale score changes from baseline
IMRT=intensity-modulated radiotherapy. EORTC HN35=European Organization for Research and Treatment of Cancer head and neck specific module HN35.

A 12 e 24 mesi: minori variazioni nel subscale score "secchezza della bocca"(questionario EORTC HN35) per IMRT vs 3DCRT (SECONDARY ENDPOINT)

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

REVIEWS SU IMRT IN HEAD AND NECK: LIVELLI EBM

LIVELLO I-II: MA PER QUALI ENDPOINTS?

Clin Transl Oncol (2008) 10:407-414
DOI 10.1007/s12094-008-0224-7

REVIEWS

2008

Clinical application of intensity-modulated radiotherapy for head and neck cancer

Olivier Ballivy · Ramón Galiana Santamaría · Alicia Lozano Borbalas · Ferrán Guedea Edo

"…the evidence for IMRT consists mainly in single-institution series and retrospective analysis…Continuing active investigation is essential for a better understanding of the complex dosimetry and biological effect of IMRT…"

2008

Review

Lancet Oncol 2008; 9: 367–375

Evidence behind use of intensity-modulated radiotherapy: a systematic review of comparative clinical studies

Liv Veldeman, Indira Madani, Frank Hulstaert, Gert De Meerleer, Marc Mareel, Wilfried De Neve

"…The generally positive findings for toxic effects and QOL are consistent with the ability of IMRT to better control the dose distribution inside (dose homogeneity & SIB) and outside (selective sparing of OARs) the PTV…"

INDIAN J CANCER **Year** : 2010 | **Volume** : 47 | **Issue** : 3 | **Page** : 267-273

2010

The role of intensity-modulated radiotherapy in head and neck cancer

SA Bhide, R Kazi, K Newbold, KJ Harrington, CM Nutting
Head and Neck Unit, The Institute of Cancer Research and The Royal Marsden Hospital, London and Surrey, United Kingdom

",,,The role of IMRT in salivary gland sparing is well established.The role of IMRT for constrictor sparing is less established.The future lies in optimally using IMRT for biologically based individualized patient treatment in order to maximize the therapeutic ratio".

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

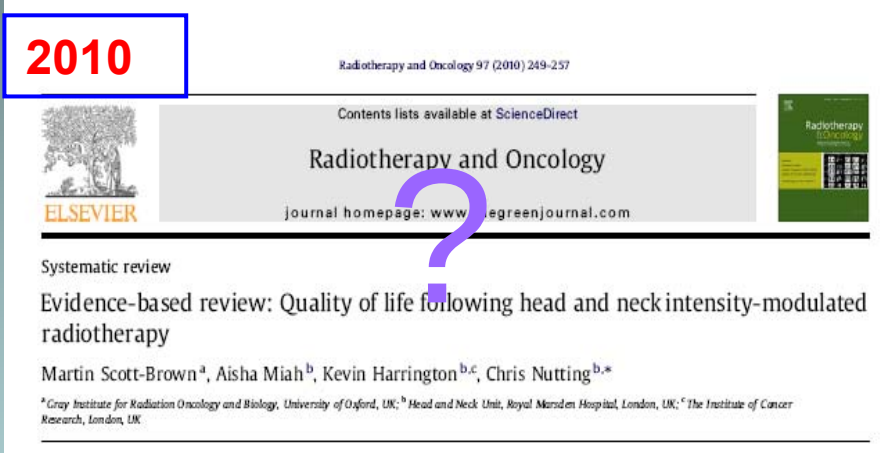
Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

REVIEWS SISTEMATICHE SULLA QUALITA' DI VITA: UNA RISPOSTA DEFINITIVA?

…PROBABILMENTE SI…ALMENO PER ALCUNI ENDPOINTS…

2010



Radiotherapy and Oncology 97 (2010) 249–257

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

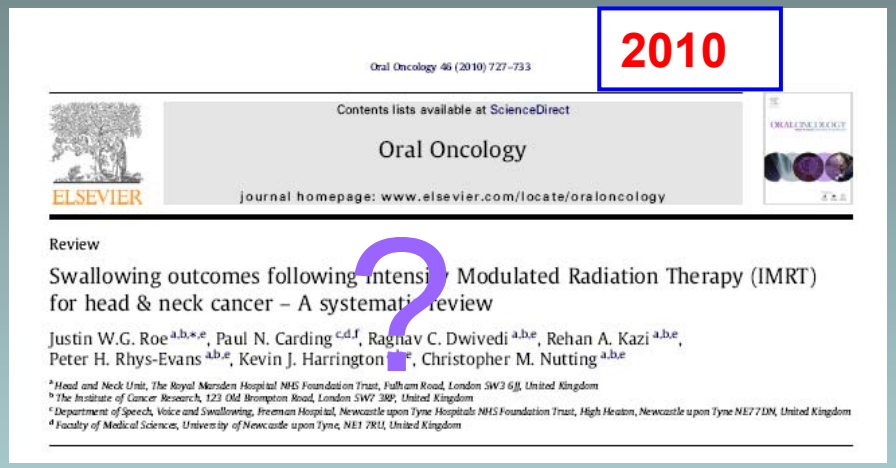
Systematic review

Evidence-based review: Quality of life following head and neck intensity-modulated radiotherapy

Martin Scott-Brown[a], Aisha Miah[b], Kevin Harrington[b,c], Chris Nutting[b,*]

[a] Gray Institute for Radiation Oncology and Biology, University of Oxford, UK; [b] Head and Neck Unit, Royal Marsden Hospital, London, UK; [c] The Institute of Cancer Research, London, UK

2010



Oral Oncology 46 (2010) 727–733

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Review

Swallowing outcomes following Intensity Modulated Radiation Therapy (IMRT) for head & neck cancer – A systematic review

Justin W.G. Roe[a,b,*,e], Paul N. Carding[c,d,f], Raghav C. Dwivedi[a,b,e], Rehan A. Kazi[a,b,e], Peter H. Rhys-Evans[a,b,e], Kevin J. Harrington[a,e], Christopher M. Nutting[a,b,e]

[a] Head and Neck Unit, The Royal Marsden Hospital NHS Foundation Trust, Fulham Road, London SW3 6JJ, United Kingdom
[b] The Institute of Cancer Research, 123 Old Brompton Road, London SW7 3RP, United Kingdom
[c] Department of Speech, Voice and Swallowing, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, High Heaton, Newcastle upon Tyne NE7 7DN, United Kingdom
[d] Faculty of Medical Sciences, University of Newcastle upon Tyne, NE1 7RU, United Kingdom

...MA:

"does it provide enough value for the additional resources involved?"

2011

ARTICLE IN PRESS

Cancer Treatment Reviews xxx (2011) xxx–xxx

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv

Antitumour Treatment

Intensity-modulated radiotherapy versus conventional and 3D conformal radiotherapy in patients with head and neck cancer: Is there a worthwhile quality of life gain?

Silke Tribius[a,*], Corinna Bergelt[b,c]

[a] Department of Radiation Oncology, University Medical Center, Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany
[b] Department of Psychosocial Medicine, Institute for Medical Psychology, University Medical Center, Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

REVIEWS SISTEMATICHE SULLA QUALITA' DI VITA

LONG-TERM GLOBAL QOL: ASPETTI CONTROVERSI

65 studi, solo 10 con dati di GQOL


2010

Radiotherapy and Oncology 97 (2010) 249–257

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Systematic review

Evidence-based review: Quality of life following head and neck intensity-modulated radiotherapy

Martin Scott-Brown[a], Aisha Miah[b], Kevin Harrington[b,c], Chris Nutting[b,*]

[a] Gray Institute for Radiation Oncology and Biology, University of Oxford, UK; [b] Head and Neck Unit, Royal Marsden Hospital, London, UK; [c] The Institute of Cancer Research, London, UK

IMRT vs 2DRT/3DCRT: eterogeneità delle dosi medie alle parotidi e degli endpoints valutati (xerostomia, funzione salivare misurata, QOL)

- *Subjective nature of QOL analysis*
- *Differences in QOL due to outcomes in the control group, IMRTgroup or both?*
- *Trial heterogeneity*
- *Time since radiotherapy*
- ***Mean parotid dose***
- *Adjustment for pre-therapy QOL scores*
- *Tumor subsite*
- *Primary vs post-op RT ± CHT*

Table 1
Mean parotid dose.

Study	Mean parotid dose in gray (Gy)				Benefit from IMRT		
	IMRT		RT		Xerostomia	Functional	QoL
			Conventional	Conformal			
Pow [15]	Ipsilateral	42 Gy (4.7; 31.3–51.2)	n.a	–	–	Yes	No
Mean (SD; range)	Contralateral	41.3 Gy (5.4; 33.1–51.8)					
Vergeer [17]	Ipsilateral	28.7 Gy (11.9)	Bilateral	–	Yes	Yes	Yes
Mean (SD)	Contralateral	23.3 Gy (11.2)	43.0 Gy				
Jabbari [11]	Ipsilateral	50 Gy (38.7–67.8)	Bilateral	–	Yes[a]	–	Yes[a]
Mean (Range)	Contralateral	21.8 Gy (14–35.5)	55.0 Gy				
Fang [9]	n.a		n.a	n.a	–	Yes[b]	Yes[b]
Fang [8]	Right	47.64 Gy (23.42–63.55)	–	Bilateral	–	No[c]	No[c]
Mean (Range)	Left	46.84 Gy (21.44–64.37)		60.0 Gy			
	Bilateral	33.7 Gy					
Graff [10]	Mean dose < 30 Gy:		n.a	–	–	Yes	No
Mean	For one or both parotids in 63.5% of patients						
	For both parotids in 23.8% of patients						
	Mean dose < 26 Gy:						
	For one or both parotids in 34.9% of patients						
McMillan [13]	Right	38.4 Gy (29.6–46.1)	–	–	–	–	–
Mean (range)	Left	40.4 Gy (29.7–53.4)					
Scrimger [16]	Total Parotid Volume	27.1 Gy (16.5)	–	–	–	–	–
Mean (SD)	Spared Parotid Volume	18.4 Gy (10.5)					
Lin [12]	n.a		–	–	–	–	–
	Right spared parotid volume	22.8 Gy (17.8–27.8)	–	–	–	–	–
Parliament [14]	Left spared parotid volume	20.9 Gy (17.9–24)					
Mean (Range)	Total Parotid Volume	30.0 Gy (26.9–33.1)					
Nutting [ASCO 2009]	Ipsilateral	45 Gy	Ipsilateral 60 Gy	–	Yes	–	n.a[d]
Mean	Contralateral	26 Gy	Contralateral 60 Gy				

SD – Standard deviation.
IMRT – Intensity modulated radiotherapy.
RT – Radiotherapy.
QoL – Quality of life.
n.a. – Not available.
[a] Clinically significant but not statistically significant.
[b] Comparing patients receiving RT therapy with [illegible] IMRT.
[c] Some benefit seen at 3 months post-radiotherapy, but no long term benefit.
[d] Results not yet published.

"…Despite overwhelming evidence that IMRT can reduce late functional deficits in H&N cancer…conflicting results with regard to QOL outcomes…"

HUMANITAS GAVAZZENI

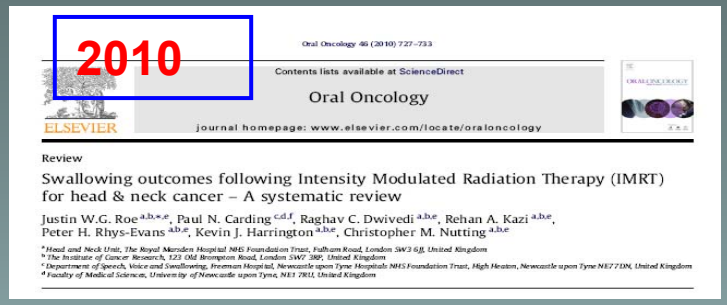
Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

REVIEWS SISTEMATICHE SULLA QUALITA' DI VITA

ENDPOINT "DEGLUTIZIONE": SERVONO ULTERIORI STUDI



2010

Oral Oncology 46 (2010) 727–733

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Review

Swallowing outcomes following Intensity Modulated Radiation Therapy (IMRT) for head & neck cancer – A systematic review

Justin W.G. Roe [a,b,*,e], Paul N. Carding [c,d,f], Raghav C. Dwivedi [a,b,e], Rehan A. Kazi [a,b,e], Peter H. Rhys-Evans [a,b,e], Kevin J. Harrington [a,b,e], Christopher M. Nutting [a,b,e]

[a] Head and Neck Unit, The Royal Marsden Hospital NHS Foundation Trust, Fulham Road, London SW3 6JJ, United Kingdom
[b] The Institute of Cancer Research, 123 Old Brompton Road, London SW7 3RP, United Kingdom
[c] Department of Speech, Voice and Swallowing, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, High Heaton, Newcastle upon Tyne NE7 7DN, United Kingdom
[d] Faculty of Medical Sciences, University of Newcastle upon Tyne, NE1 7RU, United Kingdom

16 STUDI (1998-2009) retrospettivi/prospettici

-Varie sottosedi Head & Neck

- Vari endpoints dell'indice ICF (Int. Classification of Functioning, Disability and Health Categories)

-Differenti metodi di valutazione (questionari, misurazioni strumentali)

-Diversi criteri di valutazione della disfagia

Table 2
Dysphagia evaluation quality criteria.

Dysphagia evaluation quality criteria	Results
Baseline swallowing measure used	9/16
Instrumental	3/9
Questionnaire evaluated	4/9
Instrumental & questionnaire	2/9
Toxicity criteria	1/9
Physician determined/patient reported	3/9
Post-treatment instrumental evaluation used	9/16
Videofluoroscopy	7/9
FEES	2/9
Consistent use of instrumental evaluation in all study participants	4/9
Validated rating tool used to interpret instrumental evaluation	2/9
Penetration-Aspiration scale	1/9
Oro-pharyngeal swallowing efficiency (OPSE)	1/9
Inter/intra-rater reliability studies of interpretation of instrumental studies	
Statistical interpretation	0/9
Consensus	2/9
Single rater	1/9

CONCLUSIONI:

"…potential benefits but are limited in terms of study design and outcome data"…

Table 1
Primary dysphagia studies identified detailing prospective/retrospective study design, the number of participants, site of disease, ICF classification and swallowing evaluation method.

First author	Year	Prospective/ retrospective	Number of participants	Site of disease	ICF classification	Method of evaluation
Anand[25]	2008	Prospective/ retrospective	62 *45 – IMRT* *17 – POIMRT*	Mixed (>2 sites)	Activity limitation	CTCAE v.03
Bhide[26]	2009	Prospective	37 IMRT	Mixed (>2 sites)	Activity limitation and participation restriction	RTOG late radiation morbidity score MDADI
Caglar[27]	2008	Retrospective	96 – IMRT	Mixed (>2 sites)	Impairment and activity limitation	CTCAE v.03 Swallowing Performance Scale Videofluoroscopy
Caudell[28]	2009	Retrospective	122 *62 – IMRT* *60 – CRT*	Mixed (>2 sites)	Impairment and activity limitation	Gastrostomy dependence Aspiration observed clinically or on videofluoroscopy Endoscopy
Caudell[29]	2009	Retrospective	83 – IMRT	Mixed (>2 sites)	Impairment and activity limitation	Gastrostomy dependence Aspiration observed clinically or on videofluoroscopy Endoscopy
Dirix[30]	2009	Retrospective	53 9 – IMRT 44 – 3D CRT	Mixed (>2 sites)	Activity limitation and participation restriction	RTOG late radiation toxicity score EORTC (QLQ) C30 EORTC H&N35 Performance Status Scale (PSS) MDADI
Domfeld[31]	2007	Retrospective	27 IMRT	Mixed (>2 sites)	Activity limitation and participation restriction	Head & Neck Cancer Inventory Gastrostomy dependence Food textures tolerated
Eisbruch[32]	2007	Prospective/ retrospective	95 *68 – IMRT* *22–3D CRT* *5 – CRT*	Oropharynx/ nasopharynx	Impairment, activity limitation and participation restriction	*Michigan:* Videofluoroscopy, Head & Neck Quality of Life (HN QOL) and UW QOL *Rotterdam:* PSS, EORTC H&N35, MDADI
Feng[33]	2007	Prospective	36 – IMRT	Oropharynx/ nasopharynx	Impairment, activity limitation and participation restriction	Videofluoroscopy HNQOL, UW QOL CTCAE and RTOG late radiation morbidity score
Fua[34]	2007	Retrospective	28 *25 – WF-IMRT* *8 – J-IMRT*	Nasopharynx	Activity limitation	CTCAE v.02
Levendag[35]	2007	Prospective/ retrospective	81 *46 – 2D CRT* *35 – IMRT*	Oropharynx	Activity limitation and participation restriction	PSS EORTC H&N35 MDADI
Li[36]	2009	Retrospective	39 IMRT	Mixed (>2 sites)	Impairment, activity limitation and participation restriction	Gastrostomy dependence FEES Transnasal esophagoscopy (TNE) UW QOL CTCAE v.02
Mittal[37]	2001	Prospective	39 *18 – IMRT* *21 – CRT*	Mixed (>2 sites)	Impairment, activity limitation and participation restriction	CTCAE v.02, RTOG late radiation morbidity score, SOMA scale, FACT- H&N, PSS, videofluoroscopy
Salama[38]	2008	Retrospective	95 *54 – IMRT* *41 – 3D CRT*	Mixed (>2 sites)	Impairment & activity limitation	Swallowing Performance Scale Videofluoroscopy
Teguh[39]	2008	Retrospective	95 *67 IMRT or 3DCRT* *28 – IMRT*	Oropharynx/ nasopharynx	Activity limitation and participation restriction	PSS, EORTC H&N35 & MDADI
Teguh[40]	2008	Prospective	24 *13 – IMRT* *11 – 3DCRT*	Oropharynx	Impairment, activity limitation and participation restriction	FEES PSS, EORTC H&N35 & MDADI

Abbreviations: POIMRT, post-operative IMRT; 3D CRT, 3D conformal radiotherapy; CRT, conventional radiotherapy.

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

REVIEWS SISTEMATICHE SULLA QUALITA' DI VITA

IS IT WORTHWHILE: UNA DOMANDA PROVOCATORIA?

ARTICLE IN PRESS

2011

Cancer Treatment Reviews xxx (2011) xxx–xxx

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv

Antitumour treatment

Intensity-modulated radiotherapy versus conventional and 3D conformal radiotherapy in patients with head and neck cancer: Is there a worthwhile quality of life gain?

Silke Tribius [a,*], Corinna Bergelt [b,c]

[a] Department of Radiation Oncology, University Medical Center, Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany
[b] Department of Psychosocial Medicine, Institute for Medical Psychology, University Medical Center, Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany

14 STUDI (2005-2010): 13 retrospettivi/prospettici, 1 RCT

-Varie sottosedi Head & Neck

-Questionari utilizzati: EORTC QLQ-C30 ± H&N35

-Popolazioni di pz eterogenee

-Differenti momenti di osservazione rispetto alla RT

-Vari strumenti di valutazione di QOL

CONCLUSIONI: "…IMRT was associated with statistically significant improvements in certain QOL domains vs 2DRT abd 3DCRT, particularly those relating to xerostomia…these benefits provide a rationale for the use of IMRT…"

"…prospective RCT are necessary to confirm the added value of IMRT…"

Table 1
Summary of statistically significant differences observed in EORTC QLQ-C30 and H&N35 module outcomes in studies comparing IMRT and 2DRT/3DCRT in patients with head and neck cancer. All *P*-values signify superiority of IMRT versus 2DRT/3DCRT.

	Prospective studies			Retrospective studies			
	Pow et al.[22,a]	Fang et al.[23,b]	Vergeer et al.[24,c]	Fang et al.[25,d]	Fang et al.[26,d]	Graff et al.[27,e]	Huang et al.[28,f]
Tumour type	NPC	NPC	H&N	NPC	NPC	H&N	H&N
No. of patients	51	203	241	237	356	134	307
RT techniques	IMRT versus 2DRT	IMRT versus 3DCRT	IMRT versus 3DCRT	Conformal versus 2DRT	IMRT versus 2DRT	IMRT versus 2DRT	IMRT versus 2DRT/3DCRT
EORTC QLQ-C30							
Global QoL		*P* < .05	*P* < .004	*P* < .01	*P* = .001		
Physical function				*P* < .01	*P* = .019	*P* = .01	
Role function	*P* = .035		*P* = .042				
Emotional function				*P* < .01	*P* = .017		
Cognitive function			*P* = .033	*P* < .01			
Social function			*P* < .001	*P* < .01	*P* = .011		
Fatigue		*P* < .05	*P* = .026	*P* = .02	*P* = .015		
Nausea				*P* < .01	*P* = .04	*P* = .05	
Pain				*P* < .01	*P* = .002		
Dyspnoea				*P* < .01		*P* = .01	
Insomnia			*P* = .021	*P* = .02			
Appetite loss			*P* = .018	*P* < .01	*P* = .003		
Constipation					*P* = .047		
Diarrhoea							
EORTC QLQ-C30 H&N35							
Pain			*P* = .030	*P* < .01	*P* = .031	*P* = .01	
Swallowing	*P* < .05		*P* = .042	*P* < .01	*P* = .001	*P* = .01	*P* < .01
Senses		*P* < .05		*P* < .01	*P* = .001		
Speech	*P* < .05			*P* < .01	*P* = .001		
Social eating			*P* = .011	*P* < .01	*P* = .001	*P* = .03	
Social contact				*P* < .01	*P* = .001		
Sexuality			*P* = .003		*P* = .046		
Teeth			*P* = .015	*P* < .01	*P* = .001	*P* = .02	*P* < .01
Opening mouth				*P* < .01	*P* = .001	*P* = .001	*P* < .01
Dry mouth		*P* < .05	*P* < .001	*P* < .01	*P* = .001	*P* < .0001	*P* < .01
Sticky saliva	*P* < .05		*P* = .001	*P* < .01	*P* = .001	*P* < .0001	*P* < .01
Coughing				*P* = .01	*P* = .012		
Felt ill		*P* < .05	*P* = .011	*P* < .01	*P* = .002		

2DRT, two-dimensional radiotherapy; 3DCRT, three-dimensional conformal radiotherapy; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; H&N, head and neck cancer; H&N35, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck module; IMRT, intensity-modulated radiotherapy; NPC, nasopharyngeal cancer; QoL, quality of life; RT, radiotherapy.

[a] Difference in scores at 12 months after RT.
[b] Differences at 3 months after RT.
[c] Linear effect; difference present at 6 weeks and 6 months after therapy.
[d] Median follow-up not stated.
[e] Median follow-up 22–24 months after RT.
[f] Median follow-up 3.9–7.3 years after treatment.

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

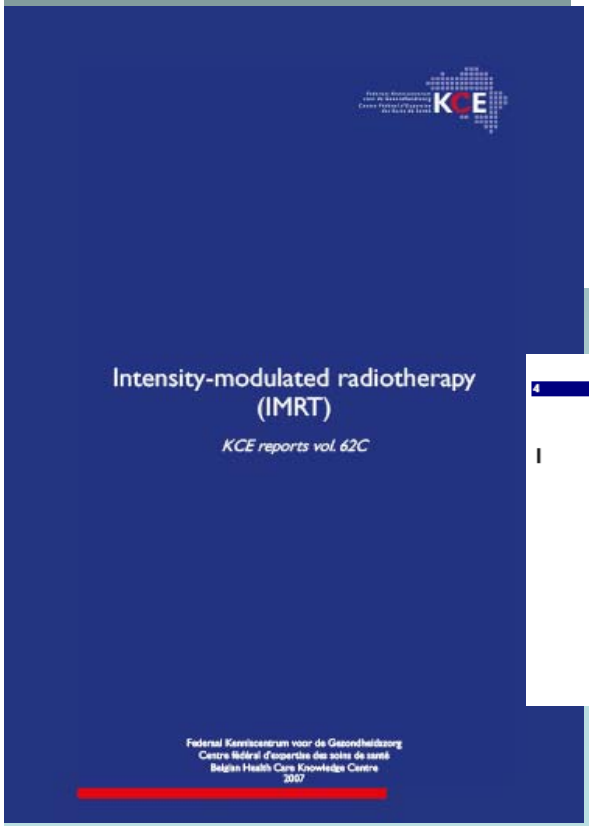
IMRT IN HEAD & NECK CANCER

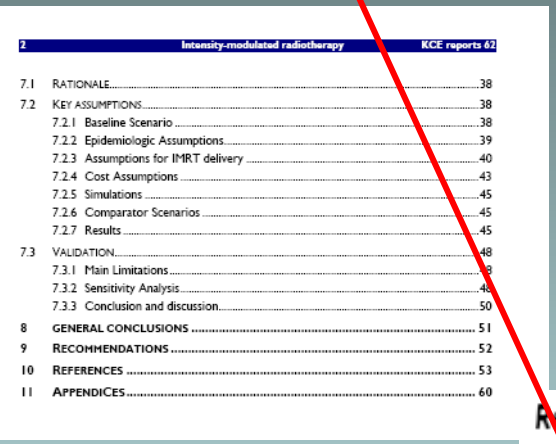
VALUTAZIONI DI HEALTH TECHNOLOGY ASSESSMENT (HTA)

RACCOMANDAZIONI CONDIVISIBILI OGGI?

The Belgian Health Care Knowledge Centre

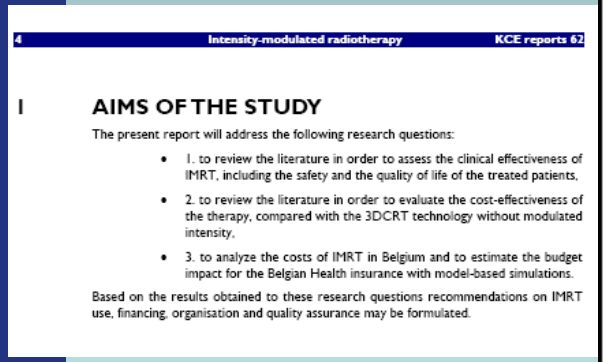
2007





2 Intensity-modulated radiotherapy KCE reports 62

7.1 RATIONALE 38
7.2 KEY ASSUMPTIONS 38
7.2.1 Baseline Scenario 38
7.2.2 Epidemiologic Assumptions 39
7.2.3 Assumptions for IMRT delivery 40
7.2.4 Cost Assumptions 43
7.2.5 Simulations 45
7.2.6 Comparator Scenarios 45
7.2.7 Results 45
7.3 VALIDATION 48
7.3.1 Main Limitations 48
7.3.2 Sensitivity Analysis 48
7.3.3 Conclusion and discussion 50
8 GENERAL CONCLUSIONS 51
9 RECOMMENDATIONS 52
10 REFERENCES 53
11 APPENDICES 60



4 Intensity-modulated radiotherapy KCE reports 62

1 AIMS OF THE STUDY

The present report will address the following research questions:

- 1. to review the literature in order to assess the clinical effectiveness of IMRT, including the safety and the quality of life of the treated patients,
- 2. to review the literature in order to evaluate the cost-effectiveness of the therapy, compared with the 3DCRT technology without modulated intensity,
- 3. to analyze the costs of IMRT in Belgium and to estimate the budget impact for the Belgian Health insurance with model-based simulations.

Based on the results obtained to these research questions recommendations on IMRT use, financing, organisation and quality assurance may be formulated.

OBJECTIVES

This "rapid health technology assessment" aims to review the literature to assess the clinical efficacy and the cost-effectiveness of intensity-modulated radiation therapy (IMRT) compared with standard 3D Conformal Radiation Therapy (3DCRT), to discuss the costs of IMRT in Belgium and to estimate the potential budget impact of IMRT on the Belgian public Health insurance by means of an economic model.

Based on the answers prompted to these research questions recommendations on IMRT use, financing, organisation and quality assurance may be formulated.

CONCLUSIONI

Recommendations

In general, more long term data are needed for IMRT treated patients, to confirm any survival advantage and to assess the increased risk of secondary malignancies in comparison with standard external radiotherapy techniques. Manufacturers and users of IMRT hardware and software should be made more aware of this risk of induction of secondary malignancies, and product improvement is to be stimulated.

As IMRT for head and neck cancer is more difficult to plan and deliver, and still an area of investigation, for the time being its use in these patients should be restricted to centres with the necessary expertise and preferentially those that are performing research in this area. The IMRT expertise at a centre could be assessed based on quality assurance measures in place, monitoring of patient outcomes and participation in clinical trials. A more appropriate financing of complex IMRT planning in head and neck cancer is to be considered.

"…IMRT…should be restricted to centres with the necessary expertise and preferentially those that are performing research…"

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

LINEE GUIDA: IMRT "STANDARD OF CARE" IN HEAD & NECK CANCER NEL REGNO UNITO

U.K. 2009

Delivering World Class Radiotherapy NHS

Intensity Modulated Radiotherapy

(IMRT)

A Guide for Commissioners

An NRIG Technology sub-group Report

- November 2009.

Published by NHS

National Cancer Action Team

Evidence Base for IMRT

Two major reviews have been published [18, 19]. These show that a large number of patients have been accrued into clinical trials but many of these have not yet been reported. The timescales are such that most aim to study acute side effects and tumour response. The published data are summarised as follows:

Head and neck cancer

There is convincing evidence that IMRT provides improved dosimetry ('conformality') compared to 3-dimensional conformal radiotherapy (3D-CRT). For example, IMRT has been shown to produce dosimetrically superior plans in head and neck cancer compared to conventional planning techniques. Reduction in xerostomia (dry mouth) has been proven in three randomised clinical trials, including one performed in the UK, by reducing the volume of parotid glands irradiated to no more than about a third of that delivered to the tumour. There are several other potential advantages including safe dose escalation, improved dose homogeneity (i.e. reduced 'hot spots' itself reducing side effects) and reduced irradiation of other radiation-sensitive organs (spinal cord, brainstem, optic nerves, mucosa etc). IMRT may also be faster than conventional conformal techniques for this patient group with consequent savings of linac time.

Conclusion

This document lays out the rationale for the implementation of IMRT as the standard of care for many radiotherapy patients. At least one third of breast cancer patients should be offered the relatively simple technique of forward planned IMRT to improve dose distribution and decrease the risk of distressing long term side effects in the conserved breast: this will apply to about 9% of all radiotherapy fractions delivered as the disease is so common. A range of other indications (e.g. head and neck cancer) will account for the use of inverse planned IMRT for about 24% of all radiotherapy fractions, making a total with breast of about 33% of treatments.

It is recommended IMRT is adopted as the standard of care within radiotherapy services for those patients that would most benefit and that funds should therefore be made available to support the operational service costs required.

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

LINEE GUIDA: IMRT "STANDARD OF CARE" PER RINOFARINGE E SENI PARANASALI IN CANADA

CANADA 2011

cancer care ontario | action cancer ontario

program in evidence-based care | programme de soins fondé sur des preuves

Evidence-Based Series #21-3-3

The Role of IMRT in Head & Neck Cancer

B. O'Sullivan, R.B. Rumble, P. Warde, and members of the IMRT Indications Expert Panel

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO),
and the Radiation Treatment Program, CCO

Report Date: January 12, 2011

The full Evidence-Based Series #21-3-3 is comprised of 3 sections and is available on the CCO Web site (http://www.cancercare.on.ca) PEBC Radiation Therapy page at:
http://www.cancercare.on.ca/toolbox/qualityguidelines/clin-program/radther/

Section 1: Guideline Recommendations
Section 2: *Evidentiary Base (Available once publication process completed*
Section 3: EBS Development Methods & External Review Process

For further information about this series, please contact:

Dr. Brian O'Sullivan, Radiation Oncologist, Head and Neck Cancer Program Leader, Princess Margaret Hospital
Professor, Department of Radiation Oncology, University of Toronto
Phone: 416-946-2125 Fax: 416-946-6556 E-mail: brian.osullivan@rmp.uhn.on.ca
or
Dr. Padraig Warde, Provincial Head, Radiation Treatment Program, CCO
Phone: 416-971-9800 x 3734 Fax: 416-971-6888 E-mail: padraig.warde@rmp.uhn.on.ca

For information about the PEBC and the most current version of all reports, please visit the CCO Web site at http://www.cancercare.on.ca/ or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775

RECOMMENDATIONS AND KEY EVIDENCE

If the reduction of xerostomia and improved quality of life are the main outcomes of interest, then IMRT is the recommended treatment for all nasopharyngeal, oropharyngeal, hypopharyngeal, laryngeal, oral cavity, and unknown primary cancers where lymph node regions requiring inclusion in the treatment volume would result in irreparable damage to salivary function if 2D EBRT or 3D EBRT were used due to their inability to maintain salivary doses within their tolerance limits (<26 Gy mean dose). The data provided are applicable to locally advanced disease but are equally applicable to early-stage disease and rare sites (e.g. salivary gland tumours) requiring RT that would otherwise damage these normal structures. In addition, these principles hold for skin malignancy where advantages in sparing normal tissue while achieving target coverage are also relevant.

Evidence

Three randomized clinical trials comparing IMRT with 2D EBRT (3-5) and other supporting evidence, including two single-arm, Phase II trials (6,7) and other studies with or without comparative data (8-15).

If blindness is to be minimized or avoided, IMRT is indicated in the definitive or adjuvant RT setting for nasal and paranasal sinus cancers or other sites where the disease is juxtaposed to the optic apparatus. The latter would include diseases such as skin malignancy and sarcomas, in addition to epithelial cancers, since ocular toxicity is often a major barrier to safe treatment planning for lesions in these locations.

Evidence

One retrospective study (9) with comparative data spanning five decades and a recent non-comparative report in paranasal sinus cancer suggesting that blindness can be virtually eliminated, while treatment efficacy seems to be improved (16). Despite the lower quality study design upon which this recommendation is based, this all-or-none outcome is considered clinically compelling and equivalent to what otherwise would be considered the highest and most compelling level of evidence (Level 1) (17).

If osteoradionecrosis is to be minimized or avoided, IMRT is indicated in the definitive or adjuvant RT of tumours in the oral cavity, oropharynx, paranasal sinuses, and nasopharynx where significant doses of RT are required and would be applied to the mandible if 2D EBRT or 3D EBRT were used.

Evidence

One retrospective study (9) with comparative data spanning five decades and two recent reports (18,19) without comparative data.

IMRT in H&N: "Gold Standard" per ridurre xerostomia, cecità e osteonecrosi

If treatment-related outcomes (local control, overall survival) are the main outcomes of interest, there are no randomized data to support or refute a recommendation of IMRT over 2D EBRT or 3D EBRT in any head and neck site. However, NPC should ordinarily be treated with IMRT based on treatment-related outcomes as should nasal and paranasal sinus cancer.

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

CLINICAL ISSUES

(QUESTIONI CLINICHE CONTROVERSE)

Clin Transl Oncol (2008) 10:407-414
DOI 10.1007/s12094-008-0224-7

REVIEWS

Clinical application of intensity-modulated radiotherapy for head and neck cancer

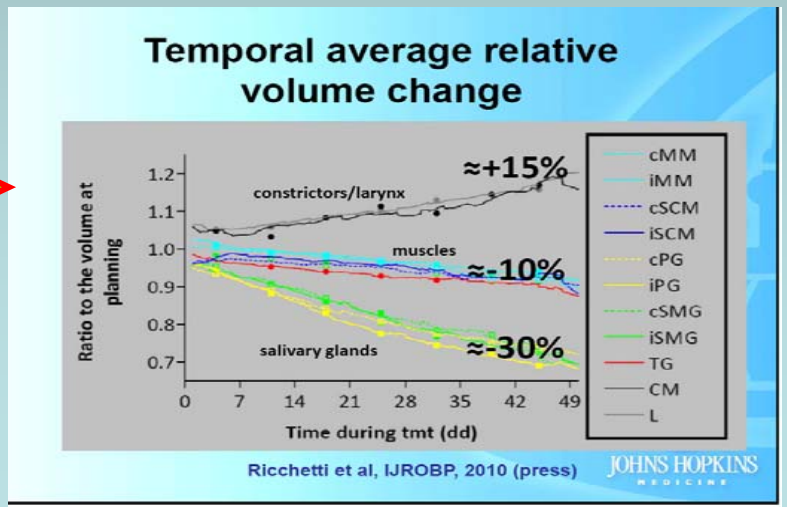
Olivier Ballivy · Ramón Galiana Santamaría · Alicia Lozano Borbalas · Ferrán Guedea Edo

TARGET DELINEATION: consensus guidelines, contouring atlases, PET scan for BTV

DOSE, FRACTIONATION & PRESCRIPTION: SIB-IMRT, several fractionation regimes, several dose prescriptions & plan evaluation criteria (ICRU 83?)

DOSE CONSTRAINTS FOR OARs: parotid & submandibular glands, oral cavity mucosa, dysphagia-related structures, potential use of biological constraints (EUD…)

GEOMETRIC UNCERTAINTIES, ORGAN MOTION & VOUME CHANGES: IGRT, ART..



HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

CONCLUSIONI: ALCUNE CERTEZZE, MOLTO LAVORO…

- IMRT è largamente utilizzata in Head & Neck e nel Rinofaringe si può ragionevolmente considerare il "gold standard" per ridurre la tossicità salivare tardiva (EBM Level I: 2 RCT).
- Il recente studio PARSPORT (RCT Fase III) mostra le stesse evidenze anche per Orofaringe/Ipofaringe (minor grado di xerostomia "late" G2+).
- L'impatto della riduzione della tossicità salivare tardiva sulla qualità di vita globale (QOL) è ancora controverso (per le difficoltà oggettive di misurazione dei vari endpoints di QOL, ma anche per l'eterogeneità degli studi sinora effettuati): sono attesi i dati di QOL degli Studi GORTEC 2004-01 (Fase III, on-going) e RTOG 0615 (Fase II, closed).
- La IMRT non ha mostrato, nelle reviews sistematiche effettuate sinora, risultati oncologici (OS, PFS, LC) inferiori alla RT convenzionale (2DRT/3DCRT), anche se una verifica con studio RCT di "non inferiorità" di IMRT vs 3DCRT, dati i notevoli numeri necessari, è difficilmente realizzabile e forse non appropriata, soprattutto alla luce dei dati dello studio PARSPORT.
- Esiste la necessità di chiarire gli aspetti controversi per ottimizzare l'utilizzazione della IMRT, specialmente in relazione alle problematiche del frazionamento (SIB-IMRT) ed alla modificazione in corso di RT degli OARs e della neoplasia.

HUMANITAS GAVAZZENI

Sabato 21 MAGGIO 2011

Incontro AIRO - AIFM Lombardia

IMRT IN HEAD & NECK CANCER

QUALCHE IDEA PER RISPONDERE ALLE "CLINICAL ISSUES"? …

ESEMPIO DI POSSIBILE RISPOSTA RAZIONALE (Regione Emilia Romagna): STUDI DI HTA

…E IN LOMBARDIA ?...

PROPOSTA "INDECENTE":

VALUTAZIONE DEL SIB-IMRT IN HEAD & NECK - SEMPLIFICAZIONE DOSIMETRICA VS OPPORTUNITA' RADIOBIOLOGICA E CLINICA

……La parola alla Dr.ssa De Marco…

SIB-IMRT IN H&N: PROBLEMATICHE APERTE

PIANIFICAZIONE

- **Necessità di una corretta identificazione di strutture linfonodali patologiche**

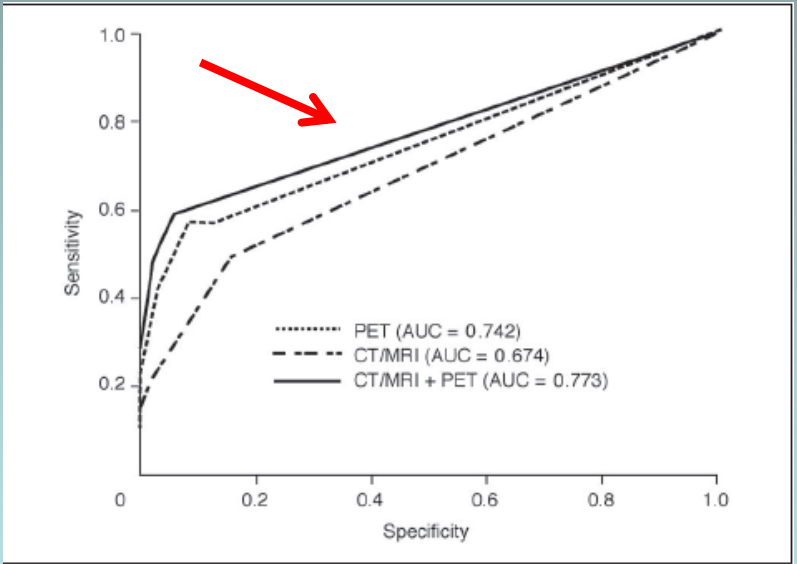
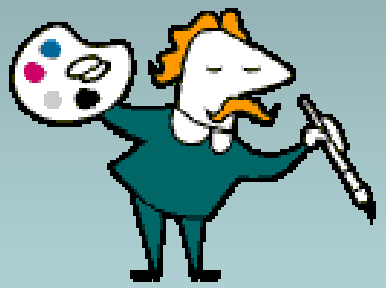
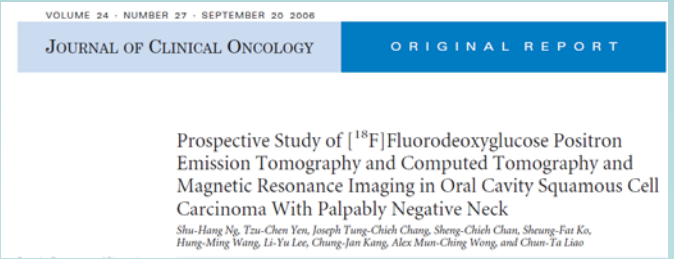


Fig 1. Receiver operating curve demonstrates a continued superiority of [^{18}F]fluorodeoxyglucose positron emission tomography ([^{18}F]FDG PET) over computed tomography (CT) or magnetic resonance imaging (MRI) as well as a modest improvement in the accuracy of visual correlation of [^{18}F]FDG PET and CT/MRI over [^{18}F]FDG PET alone. AUC, area under the curve.




VOLUME 24 · NUMBER 27 · SEPTEMBER 20 2006

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Prospective Study of [^{18}F]Fluorodeoxyglucose Positron Emission Tomography and Computed Tomography and Magnetic Resonance Imaging in Oral Cavity Squamous Cell Carcinoma With Palpably Negative Neck

Shu-Hang Ng, Tzu-Chen Yen, Joseph Tung-Chieh Chang, Sheng-Chieh Chan, Sheung-Fat Ko, Hung-Ming Wang, Li-Yu Lee, Chung-Jan Kang, Alex Mun-Ching Wong, and Chun-Ta Liao

PIANIFICAZIONE

Table 3. Nodal staging accuracy results for conventional imaging and DW-MRI

	Sensitivity per					
	LN		Cervical level		Neck Site	
Modality	CT/MRI (%)	DW-MRI (%)	CT/MRI (%)	DW-MRI (%)	CT/MRI (%)	DW-MRI (%)
Sensitivity	19/45 (42.2)	40/45 (88.9)	15/32 (46.9)	30/32 (93.8)	10/16 (62.5)	16/16 (100.0)
Specificity	143/153 (93.5)	149/153 (97.4)	92/96 (95.8)	93/96 (96.9)	14/17 (82.4)	14/17 (82.4)
Accuracy	162/198 (81.8)	189 /198 (95.5)	107/128 (83.6)	123/128 (96.1)	24/33 (72.7)	30/33 (90.9)
PPV	19/29 (65.5)	40/44 (90.9)	15/19 (78.9)	30/33 (90.9)	10/13 (76.9)	16/19 (84.2)
NPV	143/169 (84.6)	149/154 (96.8)	92/109 (84.4)	93/95 (97.9)	14/20 (70.0)	14/14 (100)

Abbreviations: LN = lymph node; PPV = positive predictive value; NPV = negative predictive value.

Results: A sensitivity of 89% and a specificity of 97% per lymph node were found for DW-MRI. Nodal staging agreement between imaging and pathology was significantly stronger for DW-MRI ($\kappa = 0.97$; 95% confidence interval [CI], 0.84–1.00) than for conventional imaging ($\kappa = 0.56$; 95% CI, 0.16–0.96; $p = 0.019$, by McNemar's test). For both imaging modalities, the absolute differences between RT volumes and those obtained by pathology were calculated. Using an exact paired Wilcoxon test, the observed difference was significantly larger for conventional imaging than for DW-MRI for nodal gross tumor volume ($p = 0.0013$), as well as for nodal clinical target volume ($p = 0.0415$) delineation.

DWI-MRI

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, pp. 761–766, 2010
Copyright © 2010 Elsevier Inc.
Printed in the USA. All rights reserved
0360-3016/10/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2009.02.068

CLINICAL INVESTIGATION **Head and Neck**

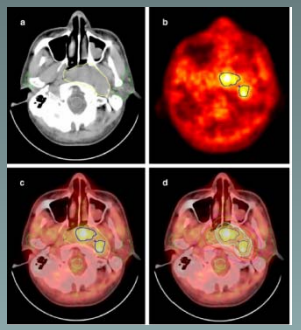
DIFFUSION-WEIGHTED MRI FOR NODAL STAGING OF HEAD AND NECK SQUAMOUS CELL CARCINOMA: IMPACT ON RADIOTHERAPY PLANNING

Piet Dirix, M.D.,* Vincent Vandecaveye, M.D.,† Frederik De Keyzer, M.Sc.,† Katya Op de beeck, M.D.,† Vincent Vander Poorten, M.D., Ph.D.,‡ Pierre Delaere, M.D., Ph.D.,‡ Eric Verbeken, M.D., Ph.D.,§ Robert Hermans, M.D., Ph.D.,† and Sandra Nuyts, M.D., Ph.D.*

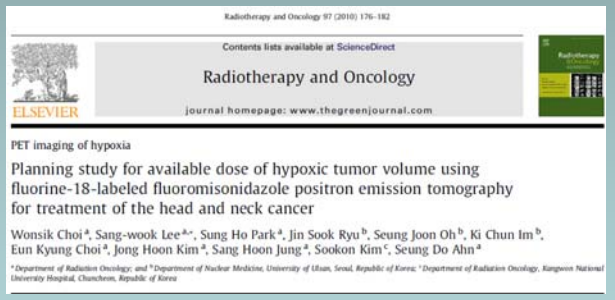
Departments of *Radiation Oncology, †Radiology, ‡Otorhinolaryngology–Head and Neck Surgery, and §Pathology, Leuvens Kankerinstituut (LKI), University Hospitals Leuven, Campus Gasthuisberg, Leuven, Belgium

PIANIFICAZIONE

Identificazione di aree ipossiche sulla sede di T e N con possibilità di escalation di dose



Results: Dose-escalation IMRT plans, delivering 30 daily doses of 2.6 Gy (total of 78 Gy) to the HTVs without increases in normal tissue doses, were feasible for six patients. Further acceptable dose escalation on HTV depended primarily on the primary tumor site and the extent of disease.
Conclusions: It was possible to dose-escalate the HTV radiation to 78 Gy in six of eight head and neck cancer patients using ^{18}F-FMISO PET/CT-guided IMRT.


Radiotherapy and Oncology 97 (2010) 176–182

Contents lists available at ScienceDirect

Radiotherapy and Oncology

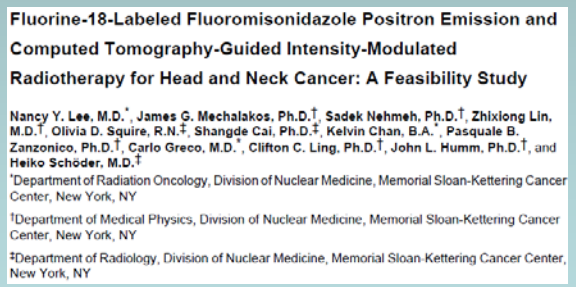
journal homepage: www.thegreenjournal.com

PET imaging of hypoxia

Planning study for available dose of hypoxic tumor volume using fluorine-18-labeled fluoromisonidazole positron emission tomography for treatment of the head and neck cancer

Wonsik Choi[a], Sang-wook Lee[a,*], Sung Ho Park[a], Jin Sook Ryu[b], Seung Joon Oh[b], Ki Chun Im[b], Eun Kyung Choi[a], Jong Hoon Kim[a], Sang Hoon Jung[a], Sookon Kim[c], Seung Do Ahn[a]

[a] Department of Radiation Oncology; and [b] Department of Nuclear Medicine, University of Ulsan, Seoul, Republic of Korea; [c] Department of Radiation Oncology, Kangwon National University Hospital, Chuncheon, Republic of Korea


Fluorine-18-Labeled Fluoromisonidazole Positron Emission and Computed Tomography-Guided Intensity-Modulated Radiotherapy for Head and Neck Cancer: A Feasibility Study

Nancy Y. Lee, M.D.*, James G. Mechalakos, Ph.D.†, Sadek Nehmeh, Ph.D.†, Zhixiong Lin, M.D.†, Olivia D. Squire, R.N.‡, Shangde Cai, Ph.D.‡, Kelvin Chan, B.A.*, Pasquale B. Zanzonico, Ph.D.†, Carlo Greco, M.D.*, Clifton C. Ling, Ph.D.†, John L. Humm, Ph.D.†, and Heiko Schöder, M.D.†

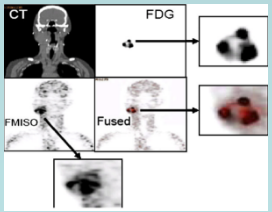
*Department of Radiation Oncology, Division of Nuclear Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY

†Department of Medical Physics, Division of Nuclear Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY

‡Department of Radiology, Division of Nuclear Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY

PET

Int J Radiat Oncol Biol Phys. 2008 January 1; 70(1): 2–13. doi:10.1016/j.ijrobp.2007.06.039.



Conclusion—It was feasible to dose escalate the GTV_h to 84 Gy in all 10 patients and in 1 patient to 105 Gy without exceeding the normal tissue tolerance. This information has provided important data for subsequent hypoxia-guided IMRT trials with the goal of further improving locoregional control in HNC patients.

PIANIFICAZIONE

Author	FS(Gy)/NF/PTD(Gy)	Tumor		Acute responding tissues	Late reacting tissues
		BED (Gy)	NTD_{2Gy}(Gy)	BED (Gy)	BED (Gy)
Conventional	2/35/70	71.5	70	56.3	116.9
Lee et al. [74]	2.1/31/65.1	68.2	66.8	53.8	112.4
	2.25/31/69.75	74.2	72.7	60.5	122.9
Kwong et al. [76]	2.17/35/76	79.1	77.4	64.7	130.1
Wolden et al. [77]	2.34/30/70.2	76.5			
Lee et al. [78]	2.4/30/72	78.9			
RTOG [87]	2.12/33/69.96	72.9			

- **2 o 3 livelli di dose?**
- **Non c' è un consenso!**
- **Non esistono trial randomizzati**
- **Evidenze limitate sulla reale efficacia di controllo della malattia con dosi da elective volume nelle regioni ad alto rischio di malattia microscopica attorno al GTV.**

Acta Oncologica, 2009; 48: 431–439

IMRT dose fractionation for head and neck cancer: Variation in current approaches will make standardisation difficult

Comparison of SIB-IMRT fractionation schedules, conventional an
miscellaneous site cancers.

Author	FS(Gy)/NF/PTD(Gy)	Tumor		Acute responding tissues	Late reacting tissues
		BED(Gy)	NTD2Gy(Gy)	BED(Gy)	BED(Gy)
Conventional	2/35/70	71.5	70	56.3	116.9
Concomitant boost					
RTOG 9003 [19]	1.8/30/54+1.5/12/18	76.9	73.9	61.5	113.4
Butler et al. [17]	2.4/25/60	68.2	66.8	56.4	108
Chao et al. [18]	2/35/70	71.5	70	56.3	116.9
Lauve et al. [81]	2.27/30/68.1	73.8	72.3	58.6	120.6
	2.36/30/70.8	77.3	75.7	64.6	127.5
	2.46/30/73.8	81.3	79.6	69.1	135.3
De Arruda et al. [80]	2.12/33/69.96	72.9	71.4	58.4	120.4
Studer et al. [83]	2/35/70	71.5	70	56.3	117.6
	2.11/33/69	72.5	71	58	119.6
	2.2/30/66	71.1	69.6	57.6	115.4
Schwartz et al. [84]	2.4/25/60	68.2	66.8	56.4	108
Guerrero Urbano et al. [85]	2.25/28/63	68.7	67.3	55.7	110.6
	2.4/28/67.2	74.3	72.7	61.8	121.3
Lee et al. [86]	2.12/33/69.96	72.9	71.4	58.4	120.4
RTOG 0022 [12]	2.2/30/66	71.1	69.6	57.6	115.4

Abbreviations for Tables 2A and B: FS(Gy)/NF/PD(Gy) fraction size/number of fraction/prescribed dose (Gy); BED(Gy), N
definitions.

OTT 6 settimane circa

Df al boost volume 66:2.36 Gy

MTD 2.36 Gy con SIB-IMRT

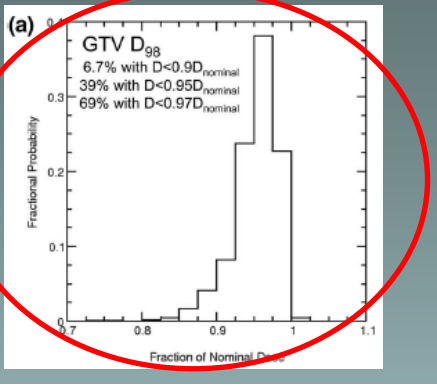
Radiobiological basis and clinical results of the simultaneous integrated boost (SIB) in intensity modulated radiotherapy (IMRT) for head and neck cancer: A review

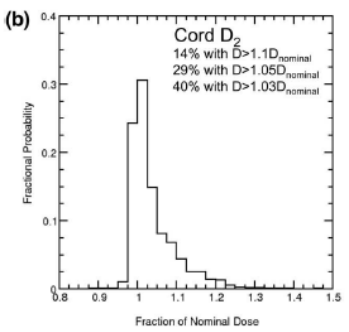
Ester Orlandi[a,*], Mauro Palazzi[a], Emanuele Pignoli[b], Carlo Fallai[a], Antonella Giostra[b], Patrizia Olmi[a]

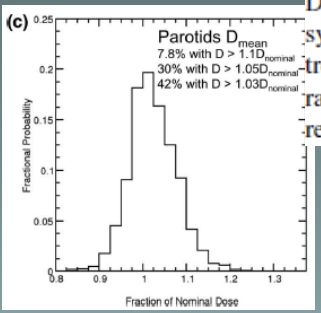
[a] Unit of Radiotherapy, Fondazione IRCCS, Istituto Nazionale dei Tumori, via Venezian 1, 20133 Milan, Italy
[b] Unit of Medical Physics, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy

Accepted 5 March 2009

EROGAZIONE







D_{mean} data. These results indicate that, in the absence of systematic setup errors, these SIB-IMRT head-and-neck treatment plans are, on average, relatively insensitive to random setup errors, since σ values exceeding 3 mm are required to produce a 3% dose error.

errors in the evaluated plan. The dose to the GTV evaluated with the inclusion of simulated 3-mm random and 3-mm systematic setup errors differed from the effective PTV by more than 5% in only 5.4% of the plans simulated. Hence, PTV dose–volume parameters are sufficiently representative of the underlying structure for dose–volume analysis. PTV concepts should be used for SIB-IMRT HNSCC patients, although the size of the margins may be less than for 3D CRT.

IGRT

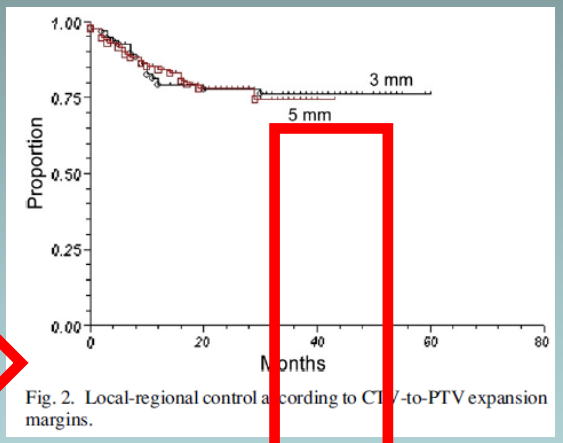


Fig. 2. Local-regional control according to CTV-to-PTV expansion margins.

Int. J. Radiation Oncology Biol. Phys., Vol. 63, No. 2, pp. 422–433, 2005
Copyright © 2005 Elsevier Inc.
Printed in the USA. All rights reserved
0360-3016/05/$–see front matter
doi:10.1016/j.ijrobp.2005.02.029

CLINICAL INVESTIGATION — Head and Neck

EFFECT OF PATIENT SETUP ERRORS ON SIMULTANEOUSLY INTEGRATED BOOST HEAD AND NECK IMRT TREATMENT PLANS

Jeffrey V. Siebers, Ph.D., Paul J. Keall, Ph.D., Qiuwen Wu, Ph.D., Jeffrey F. Williamson, Ph.D. and Rupert K. Schmidt-Ullrich, M.D.

Department of Radiation Oncology, Virginia Commonwealth University Medical Center, Richmond, VA

Conclusions: The use of 3-mm PTV expansion margins appears adequate and did not increase local-regional failures among patients treated with IMRT for head and neck cancer. These data demonstrate the safety of PTV reduction of less than 5 mm and support current protocols recommending this approach in the setting of daily IGRT. © 2010 Elsevier Inc.

ARTICLE IN PRESS
Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–7, 2010
Copyright © 2010 Elsevier Inc.
Printed in the USA. All rights reserved
0360-3016/$–see front matter
doi:10.1016/j.ijrobp.2010.07.017

CLINICAL INVESTIGATION

EVALUATION OF THE PLANNING TARGET VOLUME IN THE TREATMENT OF HEAD AND NECK CANCER WITH INTENSITY-MODULATED RADIOTHERAPY: WHAT IS THE APPROPRIATE EXPANSION MARGIN IN THE SETTING OF DAILY IMAGE GUIDANCE?

Allen M. Chen, M.D.,* D. Gregory Farwell, M.D.,† Quang Luu, M.D.,† Paul J. Donald, M.D.,* Julian Perks, Ph.D.,* and James A. Purdy, Ph.D.*

Departments of *Radiation Oncology and †Otolaryngology-Head and Neck Surgery, University of California Davis School of Medicine, Sacramento, California

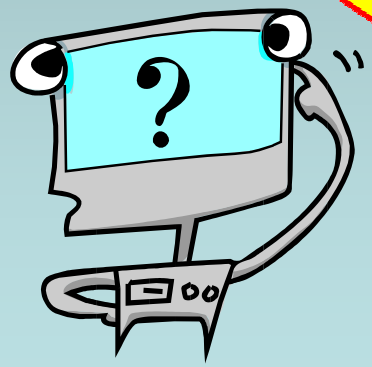
EROGAZIONE

ADAPTATIVE REPLANNING

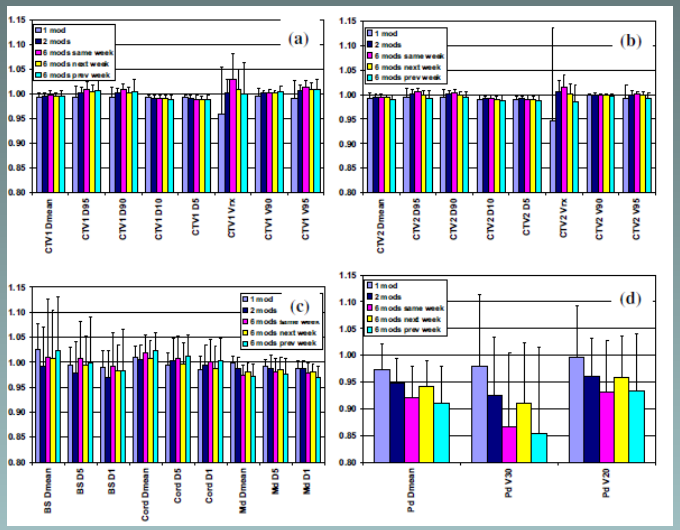
+

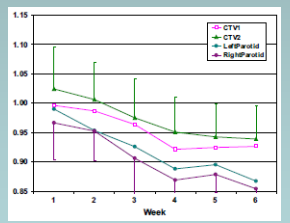
IGIMRT

→ ACCURATEZZA DEI TRATTAMENTI CON SIB



EROGAZIONE





PHYSICS CONTRIBUTION

ADAPTIVE REPLANNING STRATEGIES ACCOUNTING FOR SHRINKAGE IN HEAD AND NECK IMRT

Multiple factors affect the parotid glands doses. If no replanning is done, then the actual dose (D_{mean}) delivered to the patient will be ~10% higher than those shown in the initial plan. Reduced margins will improve the sparing of the parotid gland by ~22% from 5 to 0 mm. The ideal weekly replanning can reduce the dose by ~8% compared to treatment without replanning. Therefore, the main benefit of replanning is to preserve the sparing of the parotid shown in the initial plan. The combination of reduced margin and replanning will ideally reduce the parotid gland by ~30%, of which two-thirds comes from margin reduction and one-third from replanning. Other uncertainties during the treatment courses are worth noting, such as the rigid and nonrigid setup errors. Both can be managed and reduced with various image guidance strategies. Therefore, separate margins

Conclusions: Patients benefit most from replanning at every week interval. However, this would likely require significant time and effort and is impractical for both the planner and physician for most clinics. Therefore, this study was performed to determine the ideal time to replan HN-IMRT only once during the treatment course. The greatest benefit was seen when replanning was performed on a HCT on week 4 of treatment with a mean parotid dose reduction of 4% when compared with no replanning.

1111 **What Time is Optimal for Replanning Head and Neck IMRT (HN-IMRT)?**

Q. Wu, S. R. Nandalur, K. R. Nandalur, D. J. Krauss, P. Y. Chen, D. Yan, A. A. Martinez

William Beaumont Hospital, Royal Oak, MI

Proceedings of the 50th Annual ASTRO Meeting

SIB sempre migliore del SEQUENZIALE??

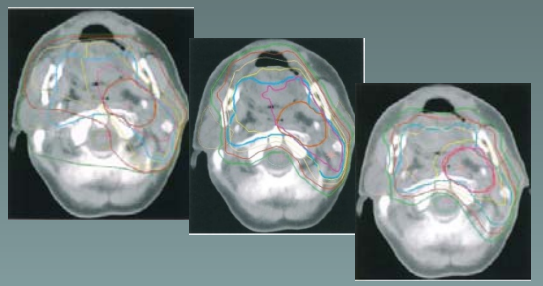


Table 3. Comparison of average doses to critical structures for H&N cases with different IMRT boost treatment techniques

	Cord	L. parotid	R. parotid	Brainstem
Sequential-IMRT$_1$				
D_{max} (Gy)	50.5 ± 3.2	73.5 ± 3.7	49.2 ± 12.9	45.2 ± 6.2
D_{mean} (Gy)	28.9 ± 9.2	52.9 ± 11.4	35.9 ± 19.8	15.4 ± 5.8
Sequential-IMRT$_2$				
D_{max} (Gy)	49.1 ± 7.4	71.9 ± 2.0	41.4 ± 20.4	42.3 ± 14.9
D_{mean} (Gy)	20.4 ± 7.4	49.1 ± 16.9	25.3 ± 15.1	12.6 ± 6.3
SIB-IMRT				
D_{max} (Gy)	48.2 ± 2.5	70.8 ± 4.4	40.2 ± 22.4	41.9 ± 9.8
D_{mean} (Gy)	21.8 ± 3.9	41.9 ± 6.0	22.8 ± 10.1	15.0 ± 7.6

ASSESSMENT OF DIFFERENT IMRT BOOST DELIVERY METHODS ON TARGET COVERAGE AND NORMAL-TISSUE SPARING

Nesrin Dogan, Ph.D., Stephanie King, C.M.D., Bahman Emami, M.D., Nateeb Mohideen, M.D., Nesa Mirkovic, M.D., Leonid B. Leybovich, Ph.D., and Anil Sethi, Ph.D.

Department of Radiation Oncology, Loyola University Chicago Medical Center, Maywood, IL

Conclusions: For equal PTV coverage, both sequential-IMRT techniques demonstrated moderately improved sparing of the critical structures. SIB-IMRT, however, markedly reduced doses to the critical structures for most of the cases considered in this study. The conformality of the SIB-IMRT plans was also much superior to that obtained with both sequential IMRT techniques. The improved conformality gained with SIB-IMRT may suggest that the dose to nontarget tissues will be lower. © 2003 Elsevier Inc.

Table 3. Data comparing the nontarget volume exposed to high levels of dose (specified in terms of nominal dose) for the conventional 3DCRT plan with different IMRT plans for the schematic HN case shown in Fig. 1.*

	Volume (cc) outside the target (tumor and nodes) regions at specified dose level or higher				
Dose level (cGy)	Conventional	Conventional with IMRT boost	Two-phase IMRT	Simultaneous integrated boost IMRT	% Difference between SIB IMRT and 2-phase IMRT
1,000	1,640	1,895	2,183	2,169	0.6
2,000	1,418	1,447	1,975	1,941	1.8
3,000	1,336	1,355	1,557	1,459	6.7
4,000	1,206	1,234	1,096	1,016	7.9
4,500	1,016	1,141	897	797	12.5
5,000	762	977	732	604	21.2
5,500	627	810	567	407	39.3
6,000	592	575	388	238	63.0
6,500	571	396	210	130	61.5
7,000	409	123	83	62	33.9

* Both plans that employ IMRT only are considerably more conformal than those that use conventional beams for all or a part of the treatment. Furthermore, the SIB plan is more conformal than the two-phase IMRT plan.

Int. J. Radiation Oncology Biol. Phys., Vol. 46, No. 3, pp. 619–630, 2000
Copyright © 2000 Elsevier Science Inc.
Printed in the USA. All rights reserved.
0360-3016/00/$–see front matter

ELSEVIER

PII S0360-3016(99)00438-1

BIOLOGY CONTRIBUTION

RADIOBIOLOGICAL CONSIDERATIONS IN THE DESIGN OF FRACTIONATION STRATEGIES FOR INTENSITY-MODULATED RADIATION THERAPY OF HEAD AND NECK CANCERS

Radhe Mohan, Ph.D.,* Qiuwen Wu, Ph.D.,* Matthew Manning, M.D.,* and Rupert Schmidt-Ullrich, M.D.*

*Department of Radiation Oncology, Medical College of Virginia, Virginia Commonwealth University and McGuire VA Hospital, Richmond, VA

SIB sempre migliore del SEQUENZIALE??

Int. J. Radiation Oncology Biol. Phys., Vol. 46, No. 3, pp. 619–630, 2000
Copyright © 2000 Elsevier Science Inc.
Printed in the USA. All rights reserved
0360-3016/00/$–see front matter

ELSEVIER

PII S0360-3016(99)00438-1

BIOLOGY CONTRIBUTION

RADIOBIOLOGICAL CONSIDERATIONS IN THE DESIGN OF FRACTIONATION STRATEGIES FOR INTENSITY-MODULATED RADIATION THERAPY OF HEAD AND NECK CANCERS

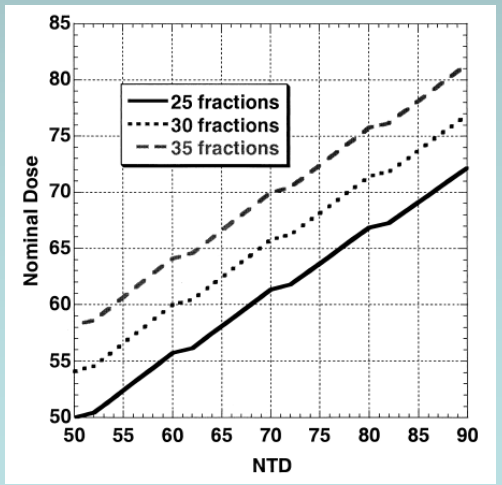
RADHE MOHAN, PH.D.,* QIUWEN WU, PH.D.,* MATTHEW MANNING, M.D.,* AND RUPERT SCHMIDT-ULLRICH, M.D.*

*Department of Radiation Oncology, Medical College of Virginia, Virginia Commonwealth University and McGuire VA Hospital, Richmond, VA

Table 5. Relationship between nominal doses and normalized total doses for various fractionation strategies

	GTV			Regional disease and electively treated volumes			NTD for normal tissues embedded in GTV*		
Strategy	Nominal dose (Gy)	Fractions and elapsed time	NTD (Gy) (fraction size)	Nominal dose (Gy)	Fractions and elapsed time	NTD (Gy) (fraction size)	Bone	Muscle	Mucosa
Conventional	70.0	35 fractions in 47 days	70	50.0	25 fx in 33 days	50.0	70	70	70
BID (MDA)	72.0	42 fx in 40 days	77.6 (1.99)	54.0	30 fx in 40 days	50.0	65.1 (1.97)	68.1 (2.00)	70.4 (2.01
BID (MCV)	72.2	40 fx in 39 days	78.1 (2.00)	51.0	27 fx in 37 days	48.3	67.6 (1.99)	69.6 (1.99)	71.1 (1.98
TID (MCV)	74.7	37 fx in 33 days	86.35 (2.01)	50.7	31 fx in 33 days	50.1	64.3 (2.01)	68.9 (2.03)	72.3 (2.01
SIB-IMRT 1	65.9	30 fx (2.20 Gy) in 40 days	70	54.0	30 fx (1.8 GY) in 40 days	50.0	70.5 (2.01)	68.5 (2.01)	67.0 (2.03
SIB-IMRT 2	71.7	30 fx (2.39 Gy) in 40 days	80	54.0	30 fx (1.8 Gy) in 40 days	50.0	81.6 (1.98)	77.2 (1.98)	74.1 (2.00
SIB-IMRT 3	77.5	30 fx (2.58 Gy) in 40 days	90	54.0	30 fx (1.8 Gy) in 40 days	50.0	93.4 (1.99)	86.4 (2.01)	81.3 (1.98
SIB-IMRT 4	70.0	35 fx (2.0 Gy) in 47 days	70	58.1	35 fx (1.66 Gy) in 47 days	50.0	70	70	70
SIB-IMRT 5 (BID)	73.6	40 fx (1.84 Gy) in 40 days	80	55.0	40 fx (1.38 Gy) in 40 days	50.0	69.5 (1.99)	71.3 (1.98)	72.6 (2.02

* The values in parentheses are doses per fraction for NTD and indicate that the conversion from a given nominal dose to NTD does not, in general, produce a value divisible exactly by 2.



"no isoeffect formula is sufficiently reliable to preempt clinical judgment, and that in the final analysis, each new fractionation schedule must be tested clinically to establish its safety."

SIB sempre migliore del SEQUENZIALE??

TOSSICITA' SALIVARE

Radiotherapy and Oncology 98 (2011) 54–56

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Head and neck radiotherapy

Sequentially delivered boost plans are superior to simultaneously delivered plans in head and neck cancer when the boost volume is located further away from the parotid glands

Emmy Lamers-Kuijper*, Wilma Heemsbergen, Anke van Mourik, Coen Rasch

The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Radiation Oncology, Amsterdam, The Netherlands

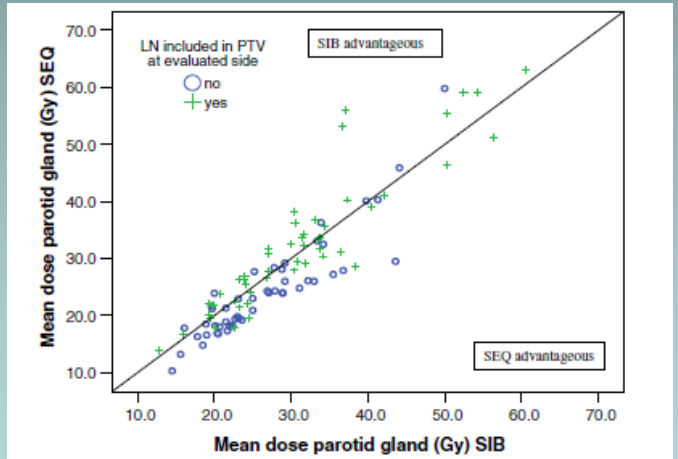


Fig. 1B. The mean dose to the parotid gland with a SEQ technique versus the mean dose with a SIB technique (Y). The dotted line indicates the situation with no difference between the SEQ and SIB technique. Lymph nodes included or not included in the PTV at the evaluated side.

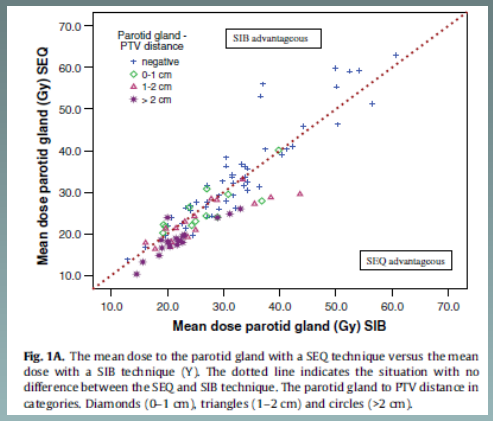


Fig. 1A. The mean dose to the parotid gland with a SEQ technique versus the mean dose with a SIB technique (Y). The dotted line indicates the situation with no difference between the SEQ and SIB technique. The parotid gland to PTV distance in categories. Diamonds (0–1 cm), triangles (1–2 cm) and circles (>2 cm).

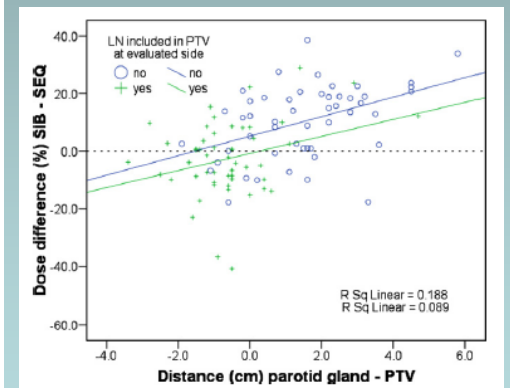


Fig. 2. The relative dose difference between the SIB and the SEQ technique versus the distance between the parotid gland and the boost PTV.

Patient and tumour characteristics.

Characteristic	N (%)
T stage	
T1	6 (12)
T2	17 (34)
T3	19 (38)
T4	8 (16)
N stage	
0	14 (28)
1	5 (10)
2	31 (62)
Location	
Nasopharynx	3 (6)
Oropharynx	35 (70)
Larynx	12 (24)
Location boost	
Left	1 (2)
Right	3 (6)
Middle	10 (20)
Middle + left	9 (18)
Middle + right	6 (12)
Middle + left + right	21 (42)
Distance boost-parotid	
<0 cm	52 (52)
0–1 cm	12 (12)
1–2 cm	16 (16)
>2 cm	20 (20)
Volume parotid gland	26.1 (11.6–66.3)

50 pz

Results of linear regression. Outcome is difference (%) between SIB and SEQ technique in planned dose to the parotid gland (50 patients, 100 evaluated parotid glands). At multivariate analysis, "LN at evaluated side" is the only parameter that remains significant ($p < 0.05$) in a model together with the variable "PTV-parotid gland distance".

Variable	B	p
Univariate		
PTV-parotid gland distance	4.2	<0.0001
T stage	−3.0	0.004
N stage	−5.2	0.001
LN involved at evaluated side (L or R), yes versus no	−13.0	<0.0001
L3 involved at evaluated side	−6.5	0.067
L2 involved at evaluated side	−12.4	<0.0001
Volume parotid gland	−0.05	0.7
Multivariate		
PTV-parotid gland distance	3.2	<0.0001
LN at evaluated side	−6.1	0.04

B = regression coefficient.

For all parotid glands with no boost PTV overlap, there is a benefit from a SEQ technique compared to a SIB technique for the gland evaluated (on average a 2.5 Gy lower dose to the parotid gland, $p < 0.001$). When the distance between gland and PTV is 0–1 cm, this difference is on average 0.8 Gy, for 1–2 cm distance 2.9 Gy and for glands with a distance greater than 2 cm, 3.3 Gy. When the lymph nodes on the eval-

SIB sempre migliore del SEQUENZIALE??

TOSSICITA' LARINGEA

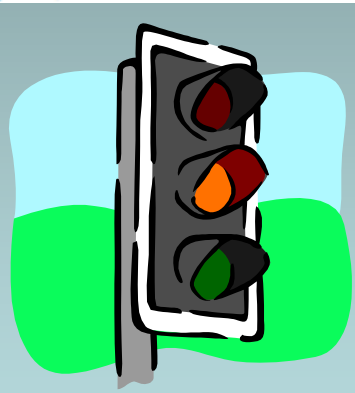
Studer et al. hanno concluso che regimi SIB con Df ≥2.2 Gy non sono raccomandati per tumori grandi che coinvolgono le strutture laringee a causa dell' alto rischio di fibrosi laringee e la necessità di tracheostomia permanente.

IMRT using simultaneously integrated boost (SIB) in head and neck cancer patients

G Studer*[1], PU Huguenin[1], JB Davis[2], G Kunz[2], UM Lütolf[1] and C Glanzmann[1]

Radiation Oncology 2006, 1:7 doi:10.1186/1748-717X-1-7

stomia risk. Larynx carcinoma patients staged T2-3N0 will in almost all cases benefit from a SEQ technique, since the primary tumour boost is located far away from the parotid glands. On the basis of the location of the boost (tumour location and lymph node level) it is possible to make a global estimation of the optimal technique choice. In our series four N0 larynx carcinoma patients had an improved dose distribution with the SEQ technique. The dis-



with oropharyngeal cancer it is more difficult to generalize about the optimal technique. Although it can be difficult to make the right choice between a SEQ or a SIB technique, there are parameters to guide which choice to make. A boost distance of more than 2 cm from a parotid gland is in almost every case beneficial for parotid gland sparing. In this case a sequentially delivered technique is the treatment of choice. In the cases where it is not clear, direct comparison of the two techniques for the individual patient before start of treatment will aid in the right choice.

Radiotherapy and Oncology 98 (2011) 51–56

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Head and neck radiotherapy

Sequentially delivered boost plans are superior to simultaneously delivered plans in head and neck cancer when the boost volume is located further away from the parotid glands

Emmy Lamers-Kuijper*, Wilma Heemsbergen, Anke van Mourik, Coen Rasch

The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Radiation Oncology, Amsterdam, The Netherlands

SIB sempre migliore del SEQUENZIALE??

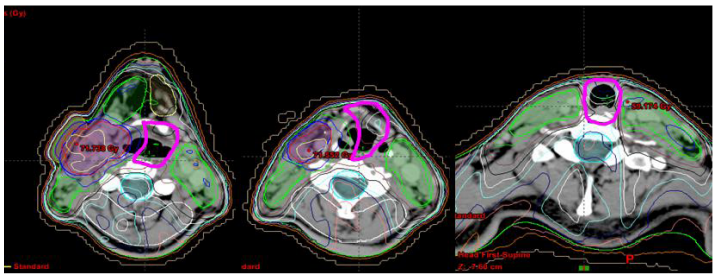
TOSSICITA' FARINGEA

Methods: 82 patients with stage III/IV squamous cell carcinoma of the larynx, oropharynx, or hypopharynx, who underwent successful definitive (n = 63, mean dose 68.9Gy) or postoperative (n = 19, mean dose 64.2Gy) simultaneous integrated boost (SIB) -IMRT either alone or in combination with chemotherapy (85%) with curative intent between January 2002 and November 2005, were evaluated retrospectively. 13/63 definitively irradiated patients (21%) presented with a total gross tumor volume (tGTV) >70cc (82-173cc; mean 106cc). In all patients, a laryngo-pharyngeal midline sparing contour outside of the PTV was drawn. Dysphagia was graded according subjective patient-reported and objective observer-assessed instruments. All patients were re-assessed 12 months later. Dose distribution to the swallowing structures was calculated.

Table 6 Results from selected series regarding late toxicity in head and neck cancer patients treated with RT ± chemotherapy

Technique	Authors [reference]	year	No of patients	median follow up (months)	stage III/IV (%)	Chemotherapy (%)	grade 3/4 late toxicity
	Chao et al [25]	2003	74	30	93	23	0
I							
	de Arruda et al [14]	2006	50	18	92	86	3 (6%)
M							
	Lee et al [17]	2006	41	31	100	100	5 (12%)
R							
	Studer et al [1]	2006	115	18	52	78	18 (15%)
T							
	present study	2010	81*	55	100	85	7 (9%)
	Denis et al [26]	2003	44	60	100	61	30 (68%)
3D-CRT							
	Huguenin et al [19]	2004	224	39	97	50	G3: 92 (41%) G4: 5 (*%)

Abbreviations: IMRT: Intensity modulated radiation therapy; 3D-CRT: three-dimensional conformal radiotherapy (*patient with previous Cobalt radiation therapy excluded).



1 Example: midline shielding as used according to our internal IMRT guidelines (pink contour, below hyoid/C3).

RESEARCH Open Access

Dysphagia in head and neck cancer patients following intensity modulated radiotherapy (IMRT)

Evangelia Peponi[1], Christoph Glanzmann[1], Bettina Willi [2], Gerhard Hu

RADIATION ONCOLOGY

Results: At the re-assessment, 32-month mean post treatment follow-up (range 16-60), grade 3/4 objective toxicity was assessed in 10%. At the 32-month evaluation as well as at the last follow up assessment mean 50 months (16-85) post-treatment, persisting swallowing dysfunction grade 3 was subjectively and objectively observed in 1 patient (1%). The 5-year local control rate of the cohort was 75%; no medial marginal failures were observed.

Conclusions: Our results show that sparing the swallowing structures by IMRT seems effective and relatively safe in terms of avoidance of persistent grade 3/4 late dysphagia and local disease control.

SIB sempre migliore del SEQUENZIALE??

TOSSICITA' MUCOSA

Clinical Oncology (2009) 21: 676–686
doi: 10.1016/j.clon.2009.07.017

Original Article

Acute Toxicities Experienced during Simultaneous Integrated Boost Intensity-modulated Radiotherapy in Head and Neck Cancers — Experience from a North Indian Regional Cancer Centre

S. Chakraborty, S. Ghoshal, V. Patil, A. Oinam, S. Suresh

Department of Radiotherapy and Oncology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

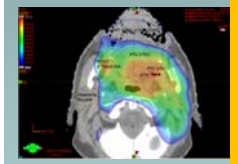
Fowler et al. hanno stimato un limite previsionale in BED di 61 Gy al di sopra del quale la tossicità mucosale acuta è intollerabile. Una Df >2.46 Gy è associata ad un' interruzione del trattamento dovuta allo sviluppo di tossicità acuta di grado 3 (in assenza di chemioterapia!).

I byte possono aumentare la dose a livello della mucosa del cavo orale

Table 10 — Single institution simultaneous integrated boost (SIB) intensity-modulated radiotherapy series reporting details of acute toxicity

Series (year) [reference]	SIB schedule	*n*	CCT (%)	Mucositis	Dermatitis	Dysphagia	Comments
Amosson *et al.* (1996–2000) [13]	60 Gy/50 Gy in 25 fractions	55	21.8	47.3% grade 3 (21.8% grade 3 pharyngitis)	NA	30.9% feeding tube	Dose evaluation to GTV/CTV
Chao *et al.* (1997–2001) [11]	Two schedules	74	27.02	40.54% grade ≥3	20.27% grade ≥3	22.97% gastrostomy	One patient had delayed mucosal ulceration
de Arruda *et al.* (1998–2004) [12]	69.6 Gy/59.4 Gy/54 Gy in 33 fractions	39 (79%)	86	38% grade 3	6% grade 3	87% PEG inserted	3.3 months median time to PEG removal
Studer *et al.* (2000–2004) [10]	Four different schedules*	115	77	15% grade 3	5% grade 3	20% grade 3 33% PEG	Seven patients experienced subacute mucosal ulcerations after treatment
Schwartz *et al.* (2002–2005) [14]	60 Gy/50 Gy in 25 fractions	49	59.2	55% grade 3	8% grade 3	20% grade 3	Treatment duration >40 days in four patients
Present series (2006–2007)	Two schedules	30	0	46.43% grade ≥3	14.3% grade 3	44.5% tube feeding	One patient had grade 4 mucositis with persistent mucosal ulceration

*Four schedules were in use: SIB 2.2 ($n=33$); SIB 2.1 ($n=44$); SIB 2.1 ($n=3$); SIB 2.0 ($n=34$). CCT, concurrent chemotherapy; NA, not available; GTV, gross tumour volume; CTV, clinical target volume; PEG, percutaneous endoscopic gastrostomy

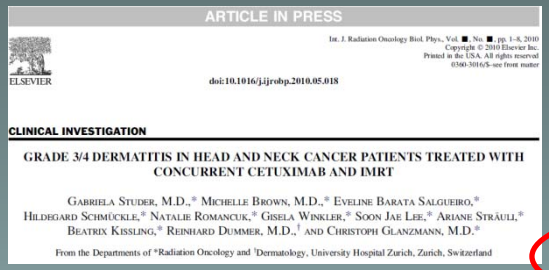


La mucosite G2 corrisponde alla zona di streaking della dose dovuta al risparmio della ghiandola parotide controlaterale al GTV

TOSSICITA' CUTANEA

- **Maschera termoplastica**
- **Natura tangenziale dei fasci fotonici in IMRT che aumentano la dose in cute**
- **Perdita di peso del paziente con riduzione dello spessore sottocutaneo che determina un incremento di dose in cute**

SIB sempre migliore del SEQUENZIALE??



ARTICLE IN PRESS

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–8, 2010
Copyright © 2010 Elsevier Inc.
Printed in the USA. All rights reserved
0360-3016/$-see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2010.05.018

CLINICAL INVESTIGATION

GRADE 3/4 DERMATITIS IN HEAD AND NECK CANCER PATIENTS TREATED WITH CONCURRENT CETUXIMAB AND IMRT

Gabriela Studer, M.D.,* Michelle Brown, M.D.,* Eveline Barata Salgueiro,* Hildegard Schmückle,* Natalie Romancuk,* Gisela Winkler,* Soon Jae Lee,* Ariane Sträuli,* Beatrix Kissling,* Reinhard Dummer, M.D.,† and Christoph Glanzmann, M.D.*

From the Departments of *Radiation Oncology and †Dermatology, University Hospital Zurich, Zurich, Switzerland

CONCLUSIONS

For HNC patients undergoing IMRT with concomitant cetuximab, this combined modality treatment:

- resulted in Grade 3/4 dermatitis in one third of all cetuximab patients
- increased the rate of severe but transient dermatitis by a factor of ~10 compared with controls treated with concomitant cisplatin only
- was associated with an increased incidence of dermatitis when the skin area was exposed to a higher radiation dose
- led to Grade 3/4 dermatitis in half the cetuximab patients irradiated with bolus

In summary, these data demonstrate that concomitant cetuximab -IMRT—including the use of bolus material—results in substantially higher rates of Grade 3/4 dermatitis than after concomitant cisplatin. These results did not translate into a change of our routine practice regarding the use of bolus material.

The presented results are most pertinent to populations where an extensive bolus is required as part of the radiation treatment.

CETUXIMAB?

Table 4. Grade 3/4 and Grade 4 dermatitis patients in the cetuximab cohort were characterized by significantly larger skin areas exposed to higher doses

Dermatitis	Mean skin area >50 Gy	Mean skin area >60 Gy
cetuximab/cisplatin	cetuximab (n)/cisplatin (n)	cetuximab (n)/cisplatin (n)
G 0-4 (n = 99)/(n = 99)	78 cm^2 (61/99)/85 cm^2 (78/99)	39 cm^2 (59/99)/36 cm^2 (60/99)
[Cetuximab only: n = 69]	[77 cm^2 (43/69)]	[38 cm^2 (41/69)]
G 0-2	61 cm^2 (31/65)/82 mL (75/96)	27 cm^2 (30/65)/36 cm^2 (57/96)
	[64 cm^2 (24/45)]	[27cm^2 (23/45)]
G 3/4 (G4 excluded)	79 cm^2 (26/30)/115 mL (3/3)	35 cm^2 (25/30)/34 cm^2 (3/3)
	[79 cm^2 (16/21)]	[35 cm^2 (15/21)]
G 4	167 cm^2 (4/4)/0/78	107 cm^2 (4/4)/0/60
	[179 cm^2 (3/3)]	[103 cm^2 (3/3)]
p value	<0.001/NS	<0.001/NS

Separately calculated data for patients treated with cetuximab only (n = 69) are shown in brackets.

	G3/4 dermatitis (n = 34)		
Cetuximab cycles	Concomitant cetuximab only (n = 69)	Concomitant cetuximab after concomitant cisplatin (n = 30)	Total (%)
1	0/4	0/0	0/4 (0)
2	1/1	2/5	3/6 (50)
3	2/6	3/13	5/19 (26)
4	2/5	4/6	6/11 (54)
5	9/19	0/5	9/24 (37)
6	6/24	1/1	7/25 (28)
7	3/9	0/0	3/9 (33)
8	1/1	0/0	1/1 (100)
Total (%)	24/69 (35)	10/30 (33)	34/99 (34)

SIB sempre migliore del SEQUENZIALE??

RT RADICALE:
26 pz

+ CHT

ORGANO	RSNA 2010	RTOG/EORTC GRADO G1	RTOG/EORTC GRADO G2	RTOG/EORTC GRADO G3
CUTE		12/26 (46.1%)	11/26 (42.3%)	3/26 (11.5%)
MUCOSA		5/26 (19.2%)	14/26 (53.8%)	7/26 (26.9%)
GHIANDOLE SALIVARI		9/26 (34.6%)	17/26 (65.3%)	0/26
FARINGE/ESOFAGO		3/26 (11.5%)	14/26 (53.8%)	9/26 (34.6%)
LARINGE		8/26 (30.7%)	2/26 (7.7%)	2/26 (7.7%)

TOSSICITA' ACUTA: ESPERIENZA DI MODENA

RT POSTOP:
21 pz

+/- CHT

	RTOG/EORTC GRADO G0	RTOG/EORTC GRADO G1	RTOG/EORTC GRADO G2	RTOG/EORTC GRADO G3	RTOG/EORTC GRADO G4
AIOCC 2011					
CUTE	0/21	13/21	8/21	0/21	0/21
MUCOSA	0/21	3/21	14/21	3/21 (14,2%)	1/21
FARINGE/ ESOFAGO	0/21	7/21	9/21	4/21 (19%)	1/21
GH.SALIVARI	2/21	4/21	15/21	0/21	0/21

SIB-IMRT: CONCLUSIONI

ASPETTI CRITICI:

- **Sede della neoplasia e volume di trattamento**
- **Frazionamento più adeguato in rapporto alla tipologia del trattamento (radicale vs postoperatorio)**
- **Associazione a chemioterapici o farmaci a bersaglio molecolare**
- **Erogazione del trattamento (IGIMRT +/- replanning)**

…Grazie per l’attenzione!!!